

Introduction to
PARASITOLOGY



Introduction to PARASITOLOGY

With Special Reference to
the Parasites of Man

9th Edition



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Preface

In 1918 I prepared a book on *Animal Parasites and Human Disease* designed to set forth interesting and important facts of human parasitology in a readable form that would make them available to a wide range of intellectually curious readers. Although not so widely taken up by the general public as anticipated, this book was at once accepted as an introductory textbook in parasitology, and year by year was adopted by more and more normal schools, universities, and medical schools throughout the country. With the fourth edition, in 1930, the book was entirely rewritten, rearranged to serve its function as a textbook more efficiently, and presented under a new title, *Introduction to Human Parasitology*. The book was, however, widely used as a general introductory textbook, so with succeeding editions its scope has been broadened to include more and more references to, or discussion of, parasites of lower animals, particularly those of importance in veterinary medicine. To reflect this extension the title was again changed in the sixth (1940) edition to its present form. The parasites of man are still most fully considered and are used as examples of their respective systematic groups, but all the parasites of veterinary importance are at least mentioned, and many of them are discussed. It would obviously be impossible to make detailed reference to parasites of other animals in an introductory textbook, but general statements are made concerning the occurrence of representatives of groups of parasites in various types of hosts. For completeness, such groups as the monogenetic flukes, strigeids, Cestodaria, etc., are discussed in this edition.

When *Animal Parasites and Human Disease* was first published, parasitology was taught in only a few universities, but there was a steady, gradual increase in the attention given to the subject up to about the beginning of World War II. I hope that this book may have played some part in the development of this gradually increasing popularity by stimulating the interest of students and by making easier the task of the teacher. During World War II and for several years thereafter, there was a very sharp upturn in interest in parasitology, due to a belated realization of the importance of the subject as a factor in world health and in the welfare of military expeditions. With the advent of

World War II, parasitology took its rightful place of prominence in the community of sciences and came of age in America. During the war parasitological problems all over the world presented themselves for immediate solution, and the neglect with which parasitology had been treated in the past became painfully apparent. There were distressingly few individuals who had had experience with even such common parasitic diseases as malaria or amebiasis, not to mention schistosomiasis, leishmaniasis, scrub typhus, etc., which few had ever even heard of. Our military forces performed a veritable miracle in correcting the situation. Not only were thousands of people trained for the efficient application of what was already known, but research in parasitology flourished as never before.

Unfortunately, in the last few years interest in parasitology in the United States, particularly unfortunately in medical schools, has tended to fall back to its inadequate prewar status. We have tended to demobilize in our fight against parasites, just as we prematurely demobilized militarily immediately after the war. We have realized our error in the latter instance, but have not yet realized it in the former, but unless we do something about our neglect of research and education in parasitology we shall inevitably regret it, and perhaps much sooner than we think. The reasons for this are outlined in Chapter 1 (Introduction) and need not be repeated here. Suffice it to say that even though parasitic diseases at present are of relatively minor importance within the boundaries of the United States, they are still of vast importance to us, and we are very short-sighted in neglecting them as we are now tending to do.

The rapid advances in knowledge in the field of parasitology, which have made it necessary to revise and largely rewrite this book every four to six years since it first appeared in 1918, have continued. In the six years that have elapsed since the eighth edition was written, unprecedented advances have been made in knowledge of the treatment and control of parasitic diseases, and innumerable other smaller additions to knowledge have been made, so again the book has been extensively revised. A number of chapters or sections have been entirely or almost entirely rewritten, and changes have been made on every page. There have been no changes in arrangement except to split the chapter on trematodes into three chapters. New and up-to-date systems of classification have been adopted throughout. An effort has been made to extend references to and consideration of parasites of veterinary importance, and the general aspects of parasitology have not been neglected. Most of the illustrations which were not new in the eighth edition have been improved or are entirely new.

As in previous editions, a chapter on spirochetes has been included,

although these organisms are now quite generally regarded as bacteria rather than Protozoa. Since the spirochetes are given inadequate treatment in most bacteriology books and are repeatedly referred to in this book in connection with their arthropod vectors, most parasitology instructors prefer to have them included. Also retained and somewhat enlarged is the section on arthropod-borne bacteria, rickettsias, and filtrable viruses, in order to give the student a more comprehensive view of these disease agents and their relations to their vectors than can be gathered from disjointed discussions of them in connection with their individual vectors.

Only enough classification and taxonomy are included to give the student an understanding of the general relationships of the parasites considered. Outlines of classification of major groups and a number of simple keys to important groups of genera and species of arthropods have been set in small type so that they do not interfere with the readability of the text and can be omitted if not considered necessary. Most students, however, will benefit from a little experience in the use of keys for identification.

Discussions of correct scientific names and synonymy have been mostly omitted as inappropriate in an introductory textbook. An effort has been made to use scientific names which are most generally accepted as correct. Some of the names used, e.g., *Entamoeba* and *Dibothriocephalus latus*, have not yet been accepted by the majority of American authors, although I feel that eventually they will be. In such cases the instructor can, of course, have his students employ the more widely used names if he wishes; no harm will have been done by calling attention to the fact that there *are* differences of opinion. Names that have long been in common use, although not now accepted as correct under rules of zoological nomenclature, are given in parentheses.

Throughout the book special emphasis has been laid on the biological aspects of the subject. Considerable space is devoted to life cycles, epidemiological factors, interrelations of parasite and host, and underlying principles of treatment and prevention, rather than on such phases as classification, nomenclature, and morphology. This book, as an introductory one, is more concerned with fundamental principles than with the details that would interest a specialist. Clinical features of the diseases caused by the parasites are not dealt with sufficiently to satisfy medical students; these are left for the professor to fill in to the extent he desires, but the underlying reasons for the pathologic effects are adequately discussed. Some therapeutic details, also, are omitted, although the availability of effective drugs, their mechanism of action, reasons for failure, effects on the host, etc., are considered.

Parasitology has grown so rapidly in recent years and covers such a wide field that it is difficult to go very far into the subject within the limits of one book. Nevertheless it is my belief that a comprehensive, integrated account of the entire field is much the most desirable method of approaching the subject at the start. Protozoology, helminthology, and medical entomology have many interrelations, and no one of them can be satisfactorily pursued very far without some knowledge of the others. For more advanced work a comprehensive textbook is too cumbersome; the subject naturally splits into its three component parts.

A brief list of references is provided at the end of each chapter for the student who wishes to pursue the subject farther. Included are books or papers which give extensive reviews or summarizations of the subjects with which they deal or which contain good bibliographies; also included are a few of the more recent contributions of importance which would not be found in bibliographies of the other works cited, and which contain information beyond that cited in the present book. In the text, references that are included in the bibliographies have the date cited in parentheses; other references are usually made in the form "Smith in 1948" It should not be too difficult for a student to trace down most of these references, if he wishes, through such journals as *Biological Abstracts*, *Helminthological Abstracts*, *Tropical Diseases Bulletin*, *Review of Applied Entomology*, *Index Medicus*, *Veterinary Bulletin*, etc.

In "Sources of Information" at the end of the book is a list of the leading journals in which important articles on parasitology frequently appear. Particular attention is called to the periodicals mentioned in the preceding paragraph. The *Tropical Diseases Bulletin* reviews practically all current work in the field of human parasitology, especially protozoology and helminthology. The *Review of Applied Entomology*, Series B, contains abstracts of all important contributions in the field of medical and veterinary entomology. The *Veterinary Bulletin* reviews important work on diseases of domestic animals. *Biological Abstracts* contains abstracts of interest in parasitology in its sections on parasitology, sanitary entomology, and in appropriate subsections under systematic zoology. The *Index Medicus* and *Quarterly Cumulative Index Medicus* list references to nearly all writings of medical interest, and the *Journal of the American Medical Association* lists references in all the leading medical journals of the world and reviews many of the more important articles. These valuable bibliographic and abstracting journals are necessary for anyone who attempts to keep pace with the progress of parasitology; without them this book could not have been kept up-to-date.

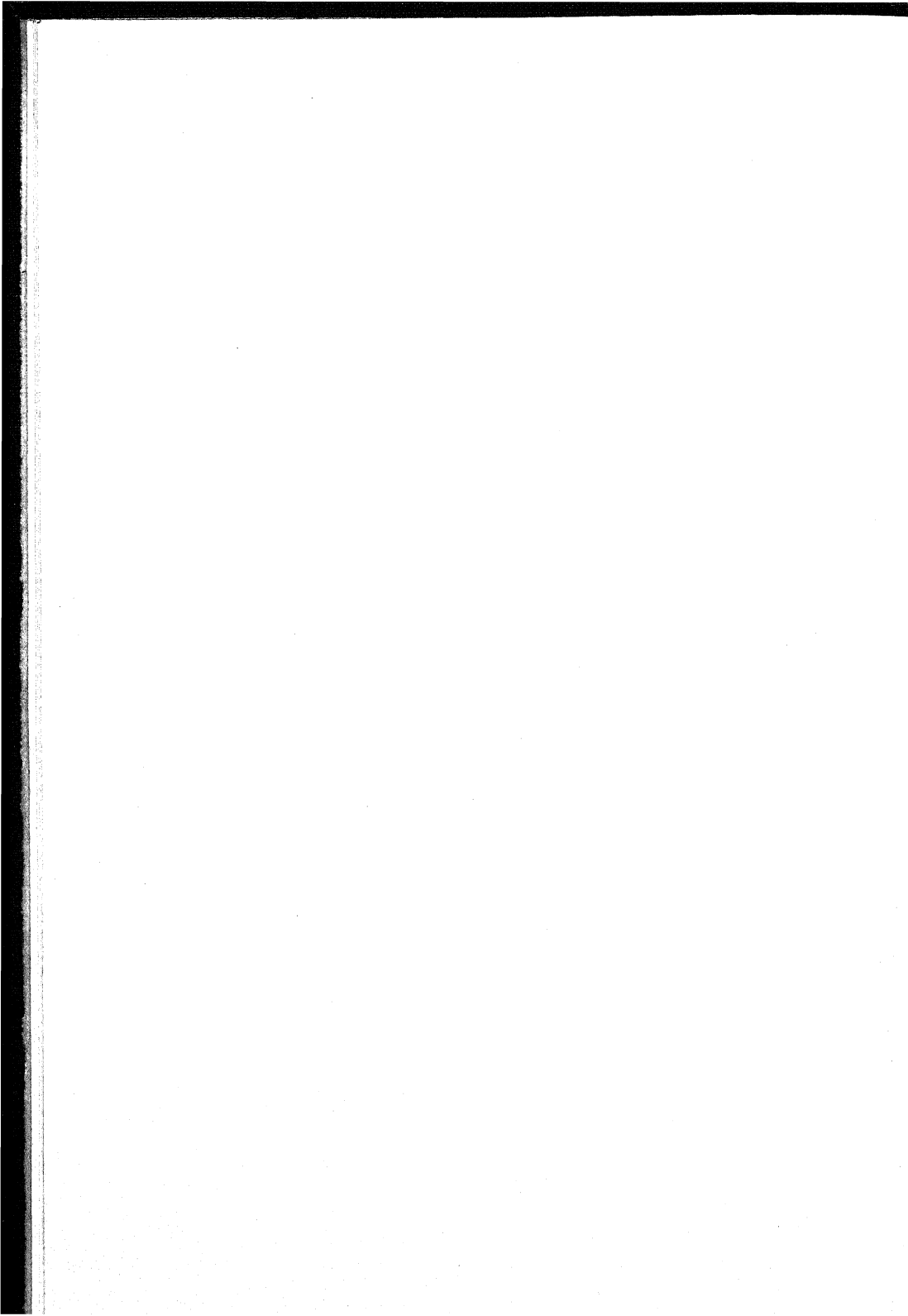
There are few if any of the journals listed under "Sources of Information" or of books or articles listed under chapter references that have not been drawn upon for help in the preparation of this book. All of them, collectively, have made the book possible, and to their authors or contributors are due therefore the thanks both of the writer and of everyone who may profit in any way from the present volume.

Most of the new illustrations in this edition were made by Mr. George Newman of the University of Texas Medical School.

In conclusion, I wish to express my appreciation of the kindness of many friends and colleagues who have helped in weeding out errors and in suggesting changes in the text. I hope that those who make use of the book will continue to offer criticisms or suggestions; they will be given careful consideration in future editions.

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The Rice Institute, Houston, Texas
May, 1955



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Introduction

One of the most appalling realizations with which every student of nature is brought face to face is the universal and unceasing struggle for existence which goes on during the life of every living organism, from the time of its conception until death. We like to think of nature's beauties, to admire her outward appearance of peacefulness, to set her up as an example for human emulation. Yet under her seeming calm there is going on everywhere—in every pool, in every meadow, in every forest—murder, pillage, starvation, and suffering.

Man often considers himself exempt from this interminable struggle for existence. His superior intelligence has given him an insuperable advantage over the wild beasts which might otherwise prey upon him; his inventive genius defies the attacks of climate and the elements; his altruism, which is perhaps his greatest attribute, protects to a great extent the weak and poorly endowed individuals from the quick extinction which is the inevitable lot of the unfit in every other species of animal on the earth. Exempt as we are to a certain extent from these phases of the struggle for existence, we have not yet freed ourselves from two other phases of it, namely, competition among ourselves, resulting in war, and our fight with parasites which cause disease.

We have made far more progress toward the latter phase than toward the former. The very inventive genius that has freed us from the great epidemics of infectious disease—cholera, plague, smallpox, yellow fever—that even in the nineteenth century spread terror in the world, has made our struggles with each other constantly more devastating and perilous, until today they threaten complete destruction of our civilization. No epidemics of disease ever threatened anything like that, even in the early days of our civilization when changing ways of life gave epidemics opportunities they never had had before in the history of the world, and when we had not yet developed countermeasures against them.

But our concern in this book is with the more auspicious struggle with parasites. Here progress has been largely one-sided, for the

slow process of evolution on which our parasitic enemies must depend is no match for the swift development of advantages afforded by human ingenuity; we purposely refrain from saying "intelligence," since the application of our ingenuity to destruction of each other can hardly be construed as intelligence. With few exceptions as far as man and his domestic animals are concerned, the enemy has been discovered, his resources and limitations known, his tactics understood, and weapons of offense and defense developed. Progress is not *always* one-sided, however. When we developed powerful chemotherapeutic drugs and deadly residual insecticides, we thought we had achieved insuperable advantages, but bacteria and trypanosomes countered with drug resistance, and flies with chemical tolerance. So we invent new chemical weapons and the parasites and vectors new defenses, but the latter seem able to work faster than our chemists.

There is another disquieting aspect of the matter. Most of our progress has been medical or chemical—development of therapeutic and prophylactic drugs, vaccines, and insecticides. These successes, as Vaucel (*WHO Newsletter*, April 1954) pointed out, along with good environmental and social conditions, have been adequate to protect the privileged Europeans and Americans even when living in undeveloped and underprivileged countries, and also the infinitesimal fraction of natives in these countries (usually called the tropics, but not confined to that area) who live European lives. Our medical successes have had much less effect on the millions of people who are living under practically the same conditions as they lived under several thousand years ago. Some of our great medical victories *have* affected backward populations, but only when they have not involved important changes in the age-old ways of life. The conquest of malaria by residual sprays is an outstanding example; houses are sprayed, but not changed, and everything else remains the same. Sleeping sickness has been greatly reduced in large areas in Africa, but all the native population had to do was to present itself for treatment. Yellow fever in South America, plague in Madagascar, kala-azar in India are other examples of the same thing. In Latin America, however, more progress has been made, concomitant with improvement in economic conditions. Houses are not merely sprayed to kill the bugs that transmit Chagas' disease; efforts are made, with spectacular success in some places in Brazil, to make the houses more suitable for human beings and less suitable for the bugs.

Because of his way of life, the white man never suffered seriously from what he considers the minor plagues of the tropics, caused by filariae, *Onchocerca*, guinea worm, hookworms, *Ascaris*, schistosomes, *Fasciolopsis*, trypanosomes, *Leishmania*, and such diseases as relapsing

fever, yaws, and tropical ulcer, to mention only a few. But these are all part and parcel of the native's daily life; he cannot avoid them, yet they incapacitate him for work, blind him, mutilate him, and make his life miserable. So little have most of these diseases affected the white man that most of them are probably totally unfamiliar to students starting to study this book.

So, in spite of some spectacular successes, the human race still has far to go in the process of emancipation from parasitic disease. It will require improvement in social and economic conditions of great masses of people—the provision of wells, latrines, decent housing, refuse disposal, proper food, shoes, and elimination of insect vectors—and also education. Of all these items, probably two stand out in importance: proper food, since malnutrition not only causes disease *per se*, but is a very large factor in ability to fight other diseases (see p. 25); and education, because only by knowing what is dangerous, and why, can mankind hope to win in the struggle with disease.

In spite of the fact that most of the parasites dealt with in this book are now relatively scarce, localized, or entirely eliminated in the United States, it does not follow that they are of little importance to us. In these days, with international travel as common as interstate travel was a generation ago, many a home-town physician has to deal with patients suffering from diseases which previously had been only names to him. Also the opportunity for dissemination of parasites or vectors entering as stowaways in airplanes, or on or in the bodies of passengers, is greater than ever before. Even when it took weeks or months to go from continent to continent, dispersal of parasites was common. Traders brought filariasis from the South Seas to Egypt, slaves brought hookworms and schistosomes from Africa to America, and trading vessels carried yellow fever from the American tropics to New York and Philadelphia. What can be expected when we can have breakfast in Colombia and supper in Florida?

But this is not all. Isolationism is gone, whether we like it or not. The world is fast becoming an economic unit, or at least two competing economic units, and a disease that affects the production of rice in Burma or meat in Argentina or coffee in Brazil inevitably affects us economically, and our stake in the welfare of undeveloped countries, large already, will inevitably increase. We have less than 10 per cent of the world's population and 8 per cent of its area, but we use 50 per cent of the produce of the Free World. We depend on foreign sources for over 40 per cent of our minerals, and 10 per cent of our other raw materials—soon it will be 20 per cent. Undeveloped areas of the world—the areas principally affected by parasitic diseases—supply 60

per cent of our imports and 40 per cent of our exports. Obviously, then, the diseases that profoundly affect the health and productivity of these areas are of very real concern to us. The diseases from which underprivileged people suffer are chronic ones, as Wright (1951) pointed out, and sick or incapacitated people are a greater drain on productivity than dead ones.

We cannot credit all our relative freedom from parasitic diseases to our own purposeful efforts. With the progress of civilization, many human parasites have gradually been falling by the wayside, but the less civilization has advanced in an area the fewer have fallen. As M. C. Hall said, the louse had its welfare imperiled when the Saturday night bath supplanted occasional immersion from falling into water; it had a struggle for survival when modern plumbing and laundering facilities laid the foundation for a daily bath even in winter, and clean clothes once a week. The housefly got a severe setback when the automobile replaced the horse, and when modern sewage systems were developed. Mosquitoes suffered with the advent of agricultural drainage and reclamation schemes. With the reduction of these vectors went reduction in the protozoan and bacterial diseases they disseminate—malaria, epidemic typhus, dysentery, etc. Of course, the advent of DDT greatly speeded up the process in some cases, but epidemic typhus had disappeared and malaria had become quite limited geographically in this country *before* that magic chemical and allied substances were discovered. Substitution of sanitary toilets for the rush-covered floors of the Middle Ages and the shaded soil of unsanitated areas spells extinction for hookworms and *Ascaris*. Cooking and refrigeration make life more precarious for *Trichinella* and *Taenia*. Improved water supplies and good sewage disposal are dangerous to most intestinal infections. To the extent that these concomitants of civilization have become part of the way of life of a people, parasitic infections have decreased even without new insecticides, new chemotherapeutics, or new vaccines. These specifically developed weapons have practically completed the white man's freedom from most of the infectious diseases that he once justifiably feared; radical changes have been wrought even since the last edition of this book was published in 1949.

For our domestic animals, on the other hand, domestication and increasing concentration have meant increasing parasitization, for they soil their table with their feces, they eat uncooked food, they drink contaminated waters from ponds and streams, they bathe only by accident, and they have hairy bodies that provide ideal playgrounds for ectoparasites. The parasite egg that had to pursue a deer or antelope

to a new bedground five miles away was out of luck, said Hall, whereas when millions of eggs are sowed on limited pastures, the parasites have all the advantage. For human parasites, increased concentration had an opposite effect owing to better opportunity for improved water, control of foods, and sanitary sewage disposal. But the parasites of the roaming deer and antelope are in a less vulnerable position than those of cattle or sheep. Some years ago the U. S. Department of Agriculture exterminated Texas fever in the United States, and eliminated *Boöphilus annulatus*, but it took years of hard and expensive work. Today warbles, hornflies, screwworms, sheep bots, and cattle lice could probably be exterminated in a fraction of the time and at much less cost.

In spite of spectacular advances in our struggle with parasites, it is obvious, then, that the battle is far from won. In 1947 Stoll made the startling estimate that there are in the world today 2200 million helminthic infections—enough for one for every inhabitant if they were evenly distributed. We have sufficient knowledge to be able to control most, though certainly not all (schistosomiasis and poliomyelitis are conspicuous exceptions) of the infectious diseases of ourselves and of our domestic animals, but they are still mostly unsubdued in vast areas of the world. There is not only need for additions to our knowledge of the causes and control of diseases, but also, and perhaps even more pressing, a need for the efficient application of what we already know. Apathy to parasitic diseases is largely the result of ignorance concerning them. Though this ignorance is most abysmal in still-primitive peoples of undeveloped countries, it is by no means absent in our own country. Some of our neighbors still think that malaria results from damp night air, that vaccination should be done away with, that animal experimentation is unjustified. After all, it is only 200 years since our Pilgrim Fathers boiled witches instead of water to control cholera!

History

Early Views. Up to the middle of the seventeenth century knowledge of parasitology was limited to recognition of the existence of a few self-asserting external parasites such as lice and fleas, and a few kinds of internal parasites which were too obvious to be overlooked, such as tapeworms, *Ascaris*, pinworms, and guinea worms. These parasites were, however, thought to be natural products of human bodies, comparable to warts or boils. Even such immortal figures in parasitology as Rudolphi and Bremser at the beginning of the nineteenth century supported this idea. In Linnaeus' time this view gradually gave way to another, that internal parasites originated from accidentally swallowed free-living organisms. Flukes, for instance, were

thought to be "landlocked" leeches or "fish"; in fact, the name fluke is said to come from the Anglo-Saxon *floc*, meaning flounder. Until the middle of the seventeenth century the necessity for parents was regarded as a handicap placed upon the higher vertebrates alone. Biology students struggling with required insect collections sometimes wonder how Noah ever succeeded in collecting all the species which must have been known even in his day for rescue in the Ark, but that was no worry of Noah's; he anticipated that insects, worms, snakes, and mice would be spontaneously generated after the flood as well as before.

Redi. The grandfather of parasitology was Francesco Redi, who was born in 1626. In the latter half of the seventeenth century he demonstrated to an unbelieving world that maggots developed from the eggs of flies, and that even *Ascaris* had males and females and produced eggs. He extended the idea of parenthood so far that it is really remarkable that its universal application, even to bacteria, had to wait for Pasteur's ingenious experiments two centuries later. Although Redi's recognition of obligatory parenthood in lower animals was his outstanding achievement, he was the first genuine parasite hunter; he searched for and found them not only in human bowels but in other human organs, in the intestines of lower animals, in the air sacs of birds, and in the swim bladders of fish.

Leeuwenhoek. This same half-century marked the origin of protozoology, for it was then that the Dutch lens grinder, Leeuwenhoek, perfected microscopes which enabled him to discover and describe various kinds of animalculae, many recognizable as Protozoa, in rain water, saliva, feces, etc.; among the organisms in feces he discovered what was probably a *Giardia*, although the first protozoan definitely recognized as a human parasite was *Balantidium coli*, discovered by Malmsten in Sweden in 1856, nearly two centuries later.

Rudolphi. In spite of the work of these pioneers, parasitology made little progress until about a century later, when Rudolphi came upon the scene. He was born in Stockholm in 1771, but did most of his work in Germany. He did for parasitology what Linnaeus did for zoologists in general; he collected and classified all the parasites known up to his time. Zeder, in 1800, recognized five classes of worms which Rudolphi named Nematoidea, Acanthocephala, Nematoda, Cestoda, and Cystica; the last had to be discarded about 50 years later when bladderworms were found to be the larval stages of the Cestoda.

Developments to 1850. During the first half of the nineteenth century numerous new species of parasites were discovered and described by Dujardin, Diesing, Cobbold, Leidy, and others. Meanwhile, observations on the life cycles of flukes and cestodes were being made.

O. F. Muller discovered cercariae in 1773 but thought they were Protozoa; Nitzsch, in 1817, recognized the resemblance of the cercarial body to a fluke and regarded the creature as a combination of a *Fasciola* and a *Vibrio*; Bojanus, in 1818, saw the cercariae emerge from "royal yellow worms" in snails, and Oken, the editor of *Isis*, in which the work was published, felt willing to wager that these cercariae were the embryos of flukes; contributions by Creplin, von Baer, Mehlis, von Siebold, von Nordman, and Steenstrup finally added enough pieces to the puzzle so that by 1842 the general pattern of the picture could readily be seen.

Meanwhile, light was also shed on the true nature of bladderworms and hydatids. As the result of observations by Redi, Tyson, Goeze, Steenstrup, von Siebold, and van Beneden, their relationships with tapeworms gradually became apparent, but up to 1850 they were generally regarded as "hydropically degenerated" as the result of development in an abnormal host into which they had accidentally strayed. It was during this period also that *Trichinella* was discovered in human flesh by Peacock (1828), and in pigs by Leidy (1846); that Dubini discovered human hookworms (1842); that Hake discovered the oöcysts of *Coccidia* in rabbits; that Gluge and Gruby discovered trypanosomes in frog blood (1842); and that Gros found the first human ameba, *Entamoeba gingivalis* (1849).

Introduction of Experimental Methods. The next important milestone in parasitology was the introduction of experimental methods. Although Abildgaard had observed as far back as 1790 that sexless tapeworms (*Ligula*) from sticklebacks would become mature when fed to birds, experimental work in parasitology really began in the middle of the nineteenth century, when Herbst (1850) experimentally infected animals with *Trichinella*, and Kuchenmeister in 1851, having the right idea about the nature of cysticerci, proceeded to prove it by feeding species of *Taenia* from rabbits to dogs and obtaining adult tapeworms. Two years later Kuchenmeister proved that bladderworms in pigs gave rise to tapeworms in man, as he had suspected because of the similarity of their heads.

These results gave a tremendous impetus to work in parasitology which has persisted to the present day, although it was temporarily eclipsed by the spectacular advances in bacteriology from about 1880 to the end of the century. The name of Leuckart stands out with especial brilliance in the early days of experimental parasitology; other shining lights in helminthology, who began their work before the beginning of the twentieth century, were Braun, Hamann, von Linstow, Looss, Lühe, and Schneider in Germany; Blanchard, Brumpt, Moniez, and Railliet in France; Cobbold and Nuttall in England; van Beneden

in Belgium; Odhner in Sweden; Fuhrmann and Zschokke in Switzerland; Galli-Valerio, Grassi, and Stossich in Italy; and Cobb, Curtice, Leidy, Theobald Smith, Stiles, and Ward in America. In protozoology there were Bütschli, Doflein, Koch, von Prowazek, Schaudinn, and von Siebold in Germany; Davaine, Mégnin, Laveran, Leger, Nicolle, Sergeant, and Aimé Schneider in France; Bruce, James, and Ross in England; and Leidy, Calkins, and Craig, in America.

Insects as Intermediate Hosts and Vectors. Following work on life cycles of helminths came the demonstration of the role of insects as intermediate hosts and vectors of parasites. Leuckart was the pioneer here when in 1867 he observed the development of *Mastophorus* (*Protospirura*) *muris* of mice, a spiruroid, in mealworms. Two years later Leuckart's pupil, Melnikov, showed that *Dipylidium* developed in dog lice, and in the same year Fedschenko observed the development of the guinea worm in *Cyclops*. The pioneer work on the role of blood-sucking arthropods was by Manson in 1878, when he observed the development of *Wuchereria bancrofti* in mosquitoes. This suggested to him the probability of mosquitoes having a comparable role in connection with malaria, and it was his advice and encouragement that led to Ross's proof of it in 1898. Meanwhile, however, two American workers, Theobald Smith and Kilbourne (1893), ingeniously worked out the transmission of Texas fever by ticks; this was the first demonstration of an arthropod as an intermediate host and vector of a protozoan parasite. Two years later Bruce showed that *Trypanosoma brucei* was transmitted by tsetse flies, and this paved the way for proof of the role of tsetse flies in sleeping sickness, though the proof of a developmental cycle in the fly was not made until 1909 by Kleine. The year 1898 brought not only the epoch-making demonstration of the role of mosquitoes in the transmission of malaria made by Ross in India and by Grassi in Italy, but also the discovery of penetration of the skin by hookworm larvae, made by Looss in Egypt. In 1900 the important discovery of the transmission of yellow fever by mosquitoes was made by the American Yellow Fever Commission in Havana. From this time on, discoveries in the life cycles and modes of transmission of parasites came thick and fast.

Chemotherapy. Important progress has also been made in the chemotherapy of parasitic infections. One of the earliest specific remedies known was quinine for malaria, introduced into Europe in the seventeenth century; with the other alkaloids of cinchona it held the field for almost 300 years. It was not until the early part of the twentieth century that other important specific drugs were discovered—Salvarsan for syphilis by Ehrlich in 1910; emetin for amebic dysentery

by Rogers in 1912; tartar emetic for leishmaniasis by Vianna in 1914; Tryparsamide for sleeping sickness by Brown and Pearce in 1920–1921. During and after World War II came the discoveries of the amazing action of antibiotics against syphilis, rickettsial diseases, and amebiasis, as well as many bacterial diseases. During this period also came the discovery of Chloroquine to replace quinine and atebirin for treatment and prophylaxis of the blood forms of malaria, and discovery of Primaquine and Daraprim for radical cure by destruction of the tissue stages of malaria parasites.

In the field of anthelmintics a few remedies—male fern, Cusso, and areca nut for tapeworms, and Santonin for nematodes—have long been known. The first great advance was made when some Italian workers established the value of thymol for hookworms in 1880. This held the field for over 30 years but was succeeded by oil of chenopodium in 1913, carbon tetrachloride in 1921, and tetrachlorethylene in 1925. Chenopodium was also very useful for *Ascaris* but was supplanted by hexylresorcinol about 1930, and since World War II has been threatened by Hetrazan and piperazine. The value of antimony compounds for schistosomiasis was discovered by McDonagh and Christopherson. Gentian violet was introduced as an anthelmintic for *Clonorchis* by Faust and Khaw in 1927, was used by deLangen for *Strongyloides* in 1928, and by Wright et al. for *Enterobius* in 1938. Also, in 1938, Harwood set a landmark when he showed the value of Phenothiazine as a veterinary anthelmintic. Hexachlorethane for *Fasciola* was introduced in Europe in 1926 but was not fully appreciated until 1941. During and after World War II atebirin was found to be effective against tapeworms, and the value of antimony and arsenic compounds for filariasis was established by Brown, Culbertson, and others. After the war Hetrazan was introduced for filariasis and onchocerciasis, and is showing evidence of being a useful drug against other helminths.

In the field of insecticides the outlook for control of nearly all arthropod parasites and arthropod-borne diseases was revolutionized by the advent of DDT and other chlorinated hydrocarbons for use as residual sprays, beginning about 1943. Development of aerosols and effective repellents has added to the troubles of insect parasites and vectors. A dramatic testimonial to the effectiveness of these developments was the voluntary dissolution of the National Malaria Society in 1951 because of the attainment of its goal—the elimination of malaria as a major public health problem (since then as an endemic disease) in the United States.

Immunity. Study of the nature and mechanism of immunity to parasitic infections is fairly recent, having been developed mainly by

American workers. The work of W. H. and L. B. Taliaferro in 1925 on the mechanism of immunity in trypanosome and malaria infections was the beginning; W. H. Taliaferro, with Cannon, Huff, Sarles, and other collaborators, has been prominent in further work in connection with immunity both to malaria and to nematode infections. A pioneer piece of work in acquired metazoan immunity was done by Blacklock and Gordon on the skin maggot (*Cordylobia*) in 1927, and another by Miller (1931) on larval tapeworms in rats. Since then, many important contributions to metazoan immunity have been made by nearly a score of American workers.

Development of Parasitology in America. In concluding this historical section a brief résumé of parasitology in America is in order. The only early naturalist in America who took an interest in this subject was Joseph Leidy; during the last half of the nineteenth century he made many and valuable contributions. He is said to have become so absorbed in the study of a worm that he entirely forgot an obstetrical case he had engaged to attend. If Joseph Leidy can be called the grandfather of American parasitology, H. B. Ward may be considered the father of it. He not only made numerous contributions of his own over a period of 50 years, but he also stimulated interest in a host of others. His position in American parasitology can best be appreciated when it is recalled that among the students who started their scientific careers under him at the University of Illinois were Ackert, Cort, Faust, Hunter, LaRue, Manter, Miller, Stunkard, Thomas, and Van Cleave. The only other university which even approaches such an output of senior modern parasitologists is Harvard, among whose sons are Kofoid, Pearse, Sawyer, Smillie, Tyzzer, Wenrich, and Ward himself. A large proportion of the ever-increasing number of the younger generation of parasitologists in America today are the scientific grandchildren of H. B. Ward.

Importance of Minor Contributions. The discoveries mentioned in this brief résumé of the history of parasitic diseases are but a few of the more conspicuous milestones on the path of progress of modern medicine as related to animal parasites. But not one of the great outstanding discoveries in the field of parasitology and preventive medicine could have been made without the aid of numerous less heralded accomplishments of hundreds of other investigators who, often without any semblance of the honor and recognition which they deserve, work for the joy of the working and feel amply repaid if they add a few pickets to the fence of scientific progress.

The formation of the American Society of Parasitologists in 1926 marked the weaning of parasitology as a science in the United States, but it was not until World War II that it really came of age and took its

rightful place in the community of sciences in America. As the writer pointed out in 1946, parasitology touches upon or overlaps so many other sciences that a parasitologist probably has to stick his nose into more different fields of knowledge than any other kind of biologist. A parasitologist, like an orchid, requires long and careful nurturing, and develops slowly (about 85 per cent of parasitologists have a Ph. D. degree). But when he comes to flower he is a rare and beautiful object, scientifically speaking, and is usually slow in going to seed.

REFERENCES

The following is a list of references of a general nature and general books on parasitology in which students who are interested may find additional information or different viewpoints. Books and references dealing with more limited subjects are listed at the end of the appropriate chapters. These references are not intended to be complete; they include only a few important or comprehensive treatises, mostly recent, to help the student who desires to do so to pursue the subject beyond the hallway to which this book may lead him. Many of the references contain bibliographies of their own which should give an entrée to the literature of the subject.

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• 2 •

Parasites in General

Nature of Parasitism. The world of animal life consists of communities of organisms which live by eating each other. In a broad sense all animals are parasites, in that they are helpless without other organisms to produce food for them. Plants alone are able to build up their body substance out of sunlight and chemicals. Herbivorous animals, when they feed on vegetation, exploit the energy of the plants for their own use. Carnivorous animals, in turn, exploit the energies of the herbivorous ones, larger carnivores exploit the smaller ones, etc., the whole series thus constituting what ecologists call a food chain; many such chains can be traced in any animal community.

But animals and plants are not preyed upon alone by successively larger forms which overpower and eat them; they are also preyed upon by successively smaller forms which destroy only small, more or less replaceable portions, or even more subtly exploit the energies of the host by subsisting on the food which the host has collected with expenditure of time and energy. Elton (1935) said: "The difference between a carnivore and a parasite is simply the difference between living upon capital and income, between the burglar and the black-mailer. The general result is the same although the methods employed are different." A man's relation to his beef cattle is essentially that of a tiger to its prey; his relation to his milk cattle and hens is essentially that of tapeworms or hookworms to their hosts. There is every gradation between parasites and carnivores, e.g., hookworms, leeches, horseflies, bloodsucking bats, and tigers; there are also all gradations between parasites and saprophytes, or organisms which live on the wastes or leftovers, e.g., rickettsias, incapable of living outside host cells; *Entamoeba histolytica*, feeding on the tissue of the host; *Trichomonas hominis*, feeding, in part, at least, on digested foods which would otherwise be converted into tissues; *Entamoeba coli*, feeding on still undigested particles and bacteria; and the coprozoic amebas, feeding on the waste fecal matter of the host.

General Relations to Hosts. The popular notion that parasites are morally more oblique in their habits than other animals, as if they were taking some unfair and mean advantage of their hosts, is, as Elton remarks, unjustified. Carnivores and herbivores have no interest in the welfare of their prey and ruthlessly destroy them; parasites, of necessity, cannot be so inconsiderate, for their welfare is intimately bound up with the welfare of the host. "A parasite's existence," says Elton, "is usually an elaborate compromise between extracting sufficient nourishment to maintain and propagate itself, and not impairing too much the vitality or reducing the numbers of its host, which is providing it with a home and a free ride." A dead host is seldom of any use to a parasite in its adult state, though it may capitalize the death of an intermediate host as a means of attaining its destination in the definitive host. Food of the right kind and in sufficient quantity is the burning question in all animal society; for parasites this resolves itself into the question of what to do when the host dies; most internal parasites, as adults, are so specialized for a protected life in the body of the host that they are unable to take any steps to deal with this situation. The result is that they make no attempt to do so and resign themselves to dying with their hosts, leaving it to their offspring to find their way to another host in order to continue the race, and, since the offspring have to run enormous risks in order to succeed, they have to be produced in correspondingly enormous numbers, running into millions.

Parasites and Food Habits. Since food is the hub of the wheel of animal life, it is natural to find that many parasites have taken advantage of the food habits of their hosts in order to propagate themselves from host to host. Intestinal Protozoa usually solve the problem by entering into a resistant cystic stage in which they can survive outside the body until they can re-enter a host with its food or water. Blood Protozoa, such as trypanosomes and malaria parasites, are adapted to live temporarily in bloodsucking insects which feed on the host and subsequently reinject them into another host. Most flukes and tapeworms lay eggs which develop into larvae in the body of an animal which the host habitually eats, or which is eaten by a third animal, which is then eaten by the definitive host. Some intestinal nematodes, such as the spiruroids, do likewise; others, such as *Ascaris*, follow the tactics of intestinal Protozoa; and still others, such as hookworms, produce self-reliant embryos which actively burrow into the skin of their hosts. Most parasitic arthropods are able to migrate from host to host when these come in contact with each other, directly or indirectly; but the bloodsucking flies have no worries about this matter, and can go at will from host to host.

The result of the dependence of parasites to such a large extent on the food habits of animals is that the food habits largely determine the nature of the parasites harbored. *Ascaris*, *Trichuris*, intestinal Protozoa, etc., are abundant where unsanitary conditions favor fecal contamination of food or water; many fluke infections of man are abundant in localities in the Far East where fish is habitually eaten raw; species of *Taenia* are abundant where pork or beef is eaten raw or partly cooked; guinea worms are common where infected *Cyclops* is ingested with drinking water; and spiruroid infections occur only accidentally in man because the human animal is nowhere habitually insectivorous in habit.

Origin of Parasitism. Parasitism, in the restricted sense of a small organism living on or in, and at the expense of, a larger one, probably arose soon after life began to differentiate in the world. It would be difficult, if not impossible, to explain step by step the details of the process of evolution by which some of the highly specialized parasites reached their present condition. Parasitism at times has probably grown out of a harmless association of different kinds of organisms, one of the members of the association, by virtue, perhaps, of characteristics already possessed, developing the power of living at the expense of the other, and ultimately becoming more and more dependent upon it.

It is easy to understand the general mechanism by which parasites of the alimentary canal were evolved from free-living organisms which were accidentally or purposely swallowed, and which were able to survive in the environment in which they found themselves, and to adapt themselves to it. It is also easy to see how some of these parasites might eventually have developed further territorial ambitions and have extended their operations beyond the confines of the alimentary canal. The development of some of the blood Protozoa of vertebrates, on the other hand, seems clearly to have taken place in two steps: first, adaptation of life in the gut of insects and, second, adaptation to life in vertebrates' blood or tissues when inoculated by hosts with skin-piercing and bloodsucking habits.

Kinds of Parasites. Parasitism is of all kinds and degrees. There are facultative parasites which may be parasitic or free-living at will, and obligatory parasites which must live on or in some other organism during all or part of their lives, and which perish if prevented from doing so. There are intermittent parasites which visit and leave their hosts at intervals. Some, as mosquitoes, visit their hosts only long enough to get a meal; others, as certain lice, leave their hosts only for the purpose of moulting and laying eggs; some ixodid ticks never leave

their host except for the final egg-laying venture from which there is no return; *Ascaris* and intestinal Protozoa live in one host from the time they hatch from an egg or a cyst until they die, but produce eggs or cysts which escape to be transferred to a new host. Some parasites are such during only part of their life cycles; botflies, for instance, are parasitic only as larvae, hookworms only as adults. The final degree of parasitism is reached in those parasites which live generation after generation on a single host, becoming transferred from host to host only by direct contact. Such are the scab mites and many species of lice. Every gradation is found among all the types of parasites mentioned above.

It is sometimes convenient to classify parasites according to whether they are external or internal. External parasites, or ectoparasites, living on the surface of the body of their hosts, suck blood or feed upon hair, feathers, skin, or secretions of the skin. Internal parasites, living inside the body, occupy the digestive tract or other cavities of the body, or live in various organs, blood, tissues, or even within cells. No sharp line of demarcation can be drawn between external and internal parasites since inhabitants of the mouth and nasal cavities, and such worms and mites as burrow just under the surface of the skin, might be placed in either category.

Definitive and Intermediate Hosts. Some parasites pass different phases of their life cycle in two or more different hosts; in a few kinds of flukes four may be involved. According to a dictionary definition, the host in which the parasite reaches sexual maturity is the definitive host and those in which it undergoes preliminary development are the intermediate hosts. Strict adherence to these definitions, however, leads to some peculiar situations among the Protozoa. For example, since the malaria parasites undergo sexual reproduction in mosquitoes, the mosquito, according to the definition, is the definitive host and man is the intermediate host. For trypanosomes, however, if Fairbairn and Culwick's work on sexual reproduction of blood trypanosomes is confirmed, tsetse flies are the intermediate hosts and man the definitive host. But in the case of *Leishmania*, in which no sexual reproduction occurs, shall we consider man or sandfly the intermediate host? Because of these difficulties, the writer prefers to use the terms definitive and intermediate for vertebrates and arthropods, respectively, in relation to protozoan parasites which alternate in their life cycles between these two types of hosts, irrespective of where the sexual reproduction, if any, occurs. An alternative is to avoid these terms altogether for Protozoa, rickettsias, etc., which multiply in both hosts, and simply to speak of vertebrate and invertebrate hosts.

Effects of Parasitism on Parasites. Aside from the toning down of their effects on the host, parasites are often very highly modified in structure to meet the demands of their particular environment. As a group, parasites have little need for sense organs and seldom have them as highly developed as do related free-living animals. Fixed parasites do not need, and do not have, well-developed organs of locomotion, if, indeed, they possess any. Intestinal parasites do not need highly organized digestive tracts, and the tapeworms and spiny-headed worms have lost this portion of their anatomy completely. On the other hand, parasites must be specialized, often to a very high degree, to adhere to or to make their way about in their particular host, or the particular part of the host in which they find suitable conditions for existence. Examples of specializations of external parasites are the compressed bodies and backward-projecting spines of fleas, which enable them to glide readily between hairs without backsliding; the clasping talons on the claws of lice; the barbed proboscides of ticks; and the tactile hairs of mites. In these same parasites can be observed marked degenerations in the loss of eyes and other sense organs, absence of wings, and sometimes reduction of legs. Internal parasites are even more peculiar combinations of degeneration and specialization. They possess all sorts of hooks, barbs, suckers, and boring apparatus, yet they have practically no sense organs or special organs of locomotion, a very simple nervous system, and sometimes, as said before, a complete absence of the digestive tube.

Still more remarkable are the specializations of parasites in their reproduction and life history to insure, as far as possible, a safe transfer to new hosts for the succeeding generations. Every structure, every function, every instinct of many of these parasites is modified, to a certain extent, for the sole purpose of reproduction. A fluke does not eat to live, it eats only to reproduce. The inevitable death of the host is the parasite's doomsday, against which it must prepare by producing all the offspring possible, in the hope that enough will survive to keep the race from extinction. The complexity to which the development of the reproductive systems may go is almost incredible. In some adult tapeworms not only does every segment bear complete male and female reproductive systems, but it may bear *two* sets of each. The number of eggs produced by many parasitic worms may run well into the millions. The complexity of the life history is no less remarkable. Not only are free-living stages interposed and intermediate hosts made to serve as transmitting agents, but also often asexual multiplications, sometimes to the extent of several generations, are passed through during the course of these remarkable experiences.

Mutual Tolerance of Hosts and Parasites. The effect of parasitism is felt by both parasite and host. A sort of mutual adaptation between the two is developed in proportion to the time that the relationship of host and parasite has existed. It is obviously to the disadvantage of internal parasites to cause the death of their host, for in so doing they destroy themselves. It is likewise to the disadvantage of external parasites, not so much to cause the death of their host, as to produce such pain or irritation as to lead to their own destruction at the hands or teeth of the irritated host. In well-established host-parasite relations the host succeeds in protecting itself against the injurious effects of the parasites, partly by developing antibodies which neutralize poisonous or injurious products of the parasites, partly by placing its blood-forming or tissue-repairing mechanisms on a plane of higher efficiency, and partly by less well-understood immune mechanisms.

Becker (1953), discussing how parasites tolerate their hosts, called attention to the many possible roles that mucoproteins and related substances of both hosts and parasites may play. One is interference with antibody action, e.g., the absorption of A_2 isoagglutinins from the blood of a host by polysaccharides excreted by invading parasitic worms which possess the A_2 antigen, and may thus protect themselves (Oliver-González and Gonzáles, 1949); and Becker's "sparing action" of duck plasma on *Plasmodium lophurae* in chicks. Another is stimulation of antibodies that may then react against the mucoprotein-producing parasites themselves or against related antigenic groups in the host's cells—a possible explanation for blackwater fever, as Oliver-González (1944) pointed out. Another may be protection of parasites against their own or their host's digestive enzymes.

A disease introduced into a new place is more destructive than in places where it has long been present. When introduced into a new species of host the delicate adjustment between host and parasite is missing, and usually either the parasite fails to survive, or else the host is severely injured or destroyed; a high degree of pathogenicity of a parasite may be considered *prima facie* evidence of a recent and still imperfect development of the host-parasite relation. An organism and the parasites which are particularly adapted to live with it may, in a way, be looked upon as a sort of compound organism. When an intermediate host is involved there is a third party added to the association, and the relationships of intermediate hosts to definitive hosts, as well as those of the parasite to each, may be important.

Modes of Infection and Transmission. The portals of entry and means of transmission of parasites are of the most vital importance from the standpoint of preventive medicine. Some parasites are spread

by direct or indirect contact with infected parts, e.g., the spirochetes of syphilis and yaws, the mouth amebas, itch mites, and, of course, free-moving ectoparasites. The parasites of the digestive system gain entrance in one of two ways. They may bore directly through the skin as larvae, e.g., hookworms. More commonly they enter the mouth as cysts or eggs, e.g., most amebas and *Ascaris*; as larvae, e.g., tape-worms; or as adults, e.g., leeches. Access to the mouth is gained in many different ways, but chiefly by four F's: feces contaminating water or food, especially vegetables; fingers; flies; or flesh of an intermediate host. The parasites of the blood and tissues usually rely on biting arthropods (insects, ticks, and mites) to transmit them from host to host, but schistosomes burrow through the skin, and guinea worms enter by the mouth.

Geographic Distribution. The distribution of parasites over the surface of the earth is dependent (1) on the presence of suitable hosts, and (2) on habits and environmental conditions which make possible the transfer from host to host. A human parasite which does not utilize an intermediate host is likely to be found in every inhabited region of the world, provided that its particular requirements with respect to habits and environmental conditions are met; and if it can also live as a parasite in other animals it may occur even beyond the limits of human habitation. Parasites such as intestinal Protozoa and itch mites, which require only slight carelessness in habits for their transfer, and are largely independent of external conditions, are practically cosmopolitan, but vary in abundance with the extent of the carelessness on which their propagation depends. *Ascaris* and *Trichuris* are only slightly more limited since they require some time outside the body to reach the infective stage, and are susceptible to heat and dryness. Hookworms are more limited, since they have to brave the dangers of the outside world as free-living organisms, unprotected by resistant egg shells; therefore, not only heat and dryness but also such factors as cold and the nature of the soil come into play.

When an intermediate host is involved, distribution is more limited, for not only must both hosts be present together, but the relations between them must be such as to favor the transfer of the parasites from one to the other. Sleeping sickness never occurs outside the range of certain species of tsetse flies, malaria beyond the range of certain species of *Anopheles*, or kala-azar outside the range of certain species of *Phlebotomus*.

Usually the distribution of the parasites is not as great as the distribution of their necessary intermediate hosts. A guinea worm not only requires both man and certain species of *Cyclops*, but it also

requires conditions under which the *Cyclops* can be reached by the embryos and under which the infected *Cyclops* can be ingested by man. Even in the presence of both man and mosquitoes, filaria may not thrive, since it must have atmospheric conditions which give it time to penetrate human skin after a mosquito has landed it there, before it dries up, and it has little chance in a place where houses and porches have mosquito-proof screens. *Clonorchis* requires not only the simultaneous presence of man, certain snails, and certain fish, but also unsanitary conditions making possible the access of eggs to the snails, a free association of infected snails and fish, and an established habit of eating raw fish. Sometimes ability to infect other hosts than man may keep alive an infection even when human habits preclude the possibility of more than occasional or rare access to the human body. No doubt the broad tapeworm would soon die out in the Canadian lakes if it were not that dogs and wild carnivores serve as reservoir hosts.

With modern transportation facilities, as remarked in the previous chapter, the possibilities of extension of the range of parasites are increased. With more frequent experimentation, parasites may find new suitable intermediate hosts, and the required environmental conditions, in new places. Yellow fever has failed, during all the past centuries, to gain access to the Far East only because the long sea journey exceeds the incubation period of the disease and makes it possible to discover cases of yellow fever and prevent them, or mosquitoes which might have fed on them, from entering. Today the danger is greater.

Resistance and Immunity

Knowledge of the means by which animals resist infectious disease, and the mechanisms by which this resistance is increased against specific organisms or their products by prior exposure to them, either naturally or by artificial means, began with Pasteur in the last half of the nineteenth century. Since then this young science of immunology has enjoyed rapid growth and today provides us with tools for preventing, ameliorating, or curing many diseases, and also with means of diagnosing them by immunological tests.

In the early days of its development this science dealt almost exclusively with bacteria or their products, or with non-living antigens, and was largely concerned with demonstration of various antigen-antibody reactions, such as toxin neutralization, agglutination, precipitation, lysis, complement fixation, increased phagocytosis (opsonification), and allergic sensitization. Most of the observations were made *in vitro*, and little attention was paid to *functional* immunity, i.e., the actual protec-

tion afforded, except in the case of toxins and antitoxins, and later of viruses and "neutralizing" antibodies.

It was well into the twentieth century before it became clear that the fundamental principles of immunity are the same for protozoans, helminths, and arthropods as for bacteria and toxins, though there are differences in degree or in details. Study of the development of resistance to metazoan parasites has been particularly fruitful in explaining functional as compared with *in vitro* demonstrations of immunity, as will be seen below.

Natural Immunity. Natural immunity to particular parasites is the birthright not only of species of animals but also of races and even individuals. It is due to genetic and environmental factors, most of which are not well understood although in some cases simple factors are concerned, such as mechanical barriers, pH, temperature, and diet. Some parasites are more tolerant of conditions in different hosts and live indiscriminately in many different ones, whereas others may be limited to one particular species (see p. 26). Parasites adapted to live in a particular species of host often thrive better in that host than in any others, but after a number of generations they may adapt themselves better to some other host (see p. 28). Natural immunity may often be broken down by such means as removal of the thyroid gland or the spleen, dietary deficiencies, injury by other infections, or other debilitating factors.

Age Resistance. Age resistance is often in reality acquired immunity, or it may be due to increased speed of development of acquired immunity. The ability to cope with infectious disease develops with age, just as does ability to digest beef steak or to solve mathematical problems. Babies cannot mobilize phagocytes or produce antibodies as efficiently as older individuals. However, there is a true age immunity of some animals to some infections. Sandground in 1928 wrote that he thought that age resistance is usually associated with abnormal or imperfectly adapted hosts; any incompatibility between host and parasite appears to become intensified with age. It is significant that most cases of human infections with "foreign" worms, belonging in other animals, are recorded in children. Ackert in 1938 found a tangible basis for age resistance of chickens to *Ascaridia* in the increase with age of intestinal goblet cells, the mucin of which he showed to have an inhibitory effect on the worms.

Acquired Immunity. Recovery from a disease confers immunity to that particular disease sometimes for life, sometimes for only a short time. Some diseases are held in check by the defenses of the host without being completely eliminated, so that they go into a relatively

quiescent chronic state, e.g., syphilis, Chagas' disease, malaria, amebiasis, etc. As long as the parasites remain in the body the host is protected against reinfection; this condition is called premunition. The host and parasite exist together in a more or less delicately balanced state. When the resistance begins to fall off, the parasites multiply sufficiently to renew it, sometimes causing a temporary relapse in the process, but the resistance may not rise sufficiently to eliminate the infection entirely. Such a situation seems to be a very common one in endemic areas not only among protozoan parasites, but among helminths as well, e.g., hookworms, schistosomes, etc., except that in this case multiplication of the parasites is replaced by renewed acquisition of them. The same general principle applies to immunity to arthropod bites; as long as there is continual exposure, most individuals are capable of developing and keeping up some degree of immunity.

The basis for all acquired immunity directed specifically against a particular parasite is probably an alteration in the structure of certain protein molecules so that they have an affinity for the antigens that stimulated them. When free in the circulation these molecules are called antibodies, but they are in the cells that produce them before they get into the circulation and may be there long after the free antibodies are gone. Almost any protein substance may act as an antigen, i.e., stimulate antibodies that will react with it.

With the exception of the simplest viruses, infectious organisms are far from being simple antigens, or even "mosaics" of a few antigens, but may contain hundreds of different antigenic substances in the form of enzymes, hormone-like substances, toxins, and other metabolic products, as well as the body proteins. In the course of a disease or after "immunization" by injection of organisms, the disintegrating dead organisms stimulate such abundant antibodies against a few of their body proteins that in an *in vitro* test these antigen-antibody reactions would completely mask any enzyme-antienzyme reactions. It would be like grinding up a cat to use as an antigen; antigens against the cat's cellular and blood proteins would certainly mask any reaction to a salivary enzyme. Yet knocking out even a single essential enzyme in a parasite might handicap it enough so that it would fall easy prey to the natural defensive mechanisms of the host. This is, in fact, what we do when we administer antibiotics or sulfa drugs; it is odd that so little attention has been paid to the possible knocking out of essential enzymes by development of specific antienzymes. Unfortunately bacteria are not easily dissected mechanically or chemically to get the pure enzymes to experiment with. It is suggestive, however, that a small number of metabolizing organisms living in a host's body may

be more effective than a thousand times the number of injected dead organisms.

This is where the advantage of metazoan parasites comes in. They can be dissected, and different tissues and organs used as antigens, as can their collected metabolic products; and they can be induced to produce immunity under conditions which preclude liberation of their body substances, making it possible to study the immunizing effects of their metabolic products independently.

Even with some Protozoa a distinction between these two types of immune reactions can sometimes be made. Taliaferro and Taliaferro demonstrated in 1922 that rats develop a reproduction-inhibiting antibody, or ablastin, as well as trypanocidal antibodies, to *Trypanosoma lewisi*. The trypanosomes are not injured in any way by the ablastin except that they are unable to reproduce, which, in the writer's opinion, is due to interference with nutrition and consequent growth; this antibody differs from others in not combining with its supposed antigen—the trypanosomes—when mixed with them. In the writer's opinion, ablastin is probably an antibody which is stimulated by and reacts with metabolic products of the trypanosome, interfering with its nutrition but not killing it. If this is true, a similar phenomenon might occur in other organisms as well, including bacteria, and explain the disappointing results from immunization with dead as compared with living vaccines.

Later (1935) the writer found that nematodes (*Nippostrongylus*) in the intestines of rats likewise had their nutrition interfered with, so that they were unable to grow normally or to reproduce. In this case it is obvious that this immune reaction could not have been directed against the parasites' body substance, but only against enzymes or metabolic products of the parasites. That this is likewise true of the migrating larvae of this worm in the parenteral phase is suggested (1) by Sarles' (1938) observation that when *Nippostrongylus* larvae are placed in immune serum, precipitates form at the external openings and in the intestine, indicating an immune reaction to metabolic products; and (2) by the fact, mentioned above, that living, migrating larvae are far more effective in producing immunity than dead ones. The development of precipitates by living larvae in immune serum has since been demonstrated for many other helminths. Campbell in 1954 demonstrated increased resistance to *Trichinella* in mice after injecting them with excretions and secretions of *Trichinella* larvae.

As immunity develops in worm infections it is manifested by (1) slower development to the adult stage; (2) stunting of growth; (3) inhibition of reproduction; (5) premature expulsion of worms already

harbored, first demonstrated by Stoll (1929) in sheep infected with *Haemonchus* (see p. 434), and termed "self-cure"; and (5) resistance to reinfection. These are all effects which might be expected if the immunity operates by interference with nutrition (Chandler, 1953b).

Acquired immunity in protozoan infections manifests itself similarly by slowing up of growth and reproduction and refractoriness to reinfection, and also by destruction of the parasites by lytic antibodies, possibly stimulated by body substances liberated from dead organisms, whenever these antibodies have access to the parasites. Usually the parasites persist longest in brain tissue. Also, intracellularly located parasites may escape. For example, early in an infection *Trypanosoma cruzi* is abundant in the blood, but in the later chronic stages only those individuals survive which quickly invade a new cell after being made homeless by the disintegration of the old one.

It is interesting to note that such worms as *Trichinella* and *Nippostrongylus*, dependent for food on the intestinal mucosa, which would be expected to become saturated with antibody before there was a high titer of antibodies in the blood, produce immunity much more quickly than bloodsuckers such as hookworms or *Haemonchus*. A similar local concentration and consequent local manifestation of immunity was demonstrated by Blacklock and Gordon in *Cordylobia* infections in the skin of guinea pigs (see p. 754). Even when antigens are liberated into the general circulation they may stimulate more or less local immunity since they may have special affinity for, and be taken up by, particular tissues. This might explain results obtained in parabiotic twins (rats) with *Nippostrongylus* infections by the writer (1935) and with *Trichinella* infections by Zaiman (1953).

It may now be assumed that acquired immunity develops against (1) all parenterally located parasites; (2) all parasites with a parenteral phase, even if it is only temporary invasion of the mucosa (e.g., esophagostomes and cysticercoids of *Hymenolepis nana*); and (3) parasites that break the mucosa sufficiently to inject antigens from the mouth while feeding, as trematodes and most nematodes do. The tapeworms and acanthocephalans are exceptional in that some of them, at least, fail to get any antigen inoculated into their hosts and thus fail to stimulate any specific immunity. Refractoriness of these parasites to reinfection was shown by Chandler (1939) and Burlingame and Chandler (1941) to be due entirely to a crowding effect. A unique situation exists in the case of the tapeworm, *Hymenolepis nana*, which may infect its host either as eggs, in which case there is a parenteral cysticercoid phase in the villi, or as cysticercoids developed in beetles, in which case there is no parenteral phase and, as might be expected, no specific

immunity. Heyneman (1954) showed, however, that immunity produced by an egg infection not only protects the host against subsequent egg infections, but also affects worms in the intestinal lumen resulting from feeding of cysticercoids.

Relation of Diet to Immunity. A factor of paramount importance in connection with development of acquired immunity is diet. Adequate protein of good quality is necessary for production of antibodies and phagocytes. Even a reasonably good diet may be inadequate if one or more of the following conditions exist—low protein, insufficient calories, poor vitamin content, growth (in young animals or children), loss of blood, or pregnancy. With inadequate protein, failure of immunity allows for unimpeded multiplication of parasites or continued acquisition of new ones, which further lowers resistance of the host and establishes a vicious cycle. On the other hand, one may go so far as to say that severe chronic nematode or trematode infections are probably impossible in a well-nourished and otherwise healthy animal except under conditions of very heavy exposure to infection before there has been time for immunity to develop (Chandler, 1953a). A striking demonstration of this was made by Foster and Cort (1932, 1935), working with hookworm infections in dogs. In the writer's opinion, the level of infection with hookworms in a community, for example, is more a measure of the dietary conditions than it is of exposure to infection. The poorer the diet, the more severe the infection must become before protein is diverted to antibody production. The corollary of this is that to a large degree severe chronic parasitism with nematodes, and perhaps many other parasites as well, is a symptom of poor nutrition.

For most adult tapeworms, which do not stimulate antibody production, the nutritional effects are different. A good diet does not adversely affect the worms but *does* help the host, permitting him to feed the worms as well as himself without injurious loss of proteins and vitamins.

Tolerance to Injurious Effects. In the foregoing paragraphs we have considered principally the immunity brought about by reactions against the parasites which result in their death or interference with their metabolism. In addition, however, there is a development of tolerance to the injurious products of parasites, or increased efficiency in repairing damage done by them, which protects the host without injuring the parasites. Persons losing blood from hookworm infections place their blood-forming mechanism on a plane of increased activity and efficiency; animals exposed to injury by the toxic products of screw-worms develop the ability to neutralize these products and render them less harmful; and persons exposed to worm infections increase the

number of the special white blood corpuscles called eosinophiles, which are somehow concerned with the neutralization of injurious products of the worms. This eosinophilia is a very characteristic feature of worm infections, particularly parenteral ones; failure to respond to parenteral invasions of worms by an increase in eosinophiles indicates that the defensive mechanism of the host is not functioning efficiently.

Host Specificity

Intimately bound up with the question of resistance of hosts and the mutual adaptation of host and parasite to each other is the question of limitation of parasites to particular hosts. In order for a parasite to live habitually in a host two conditions must be met: (1) a dependable means of transfer from individual to individual, and (2) ability to thrive in the individual when it gets there. It is the interplay of these two factors which determines in what hosts a parasite lives. Every parasite, of course, has at least one species of host, and sometimes several, in which these conditions are satisfactorily met; otherwise it would cease to exist. Usually there are other hosts in which one or both conditions are only occasionally met, in which case "accidental" parasitism results. Man's failure to utilize insects as food, except accidentally, relieves him from *common* infection with parasites such as spirurids, *Acanthocephala*, and most tapeworms, which encyst in insects as intermediate hosts, although he is susceptible to a great many of these parasites when they *do* get access to him. On the other hand, man must commonly be exposed to infection with such parasites as bird malaria, animal schistosomes, dog and cat hookworms, and bird filariae, yet infection rarely or never occurs, because the parasites do not find suitable conditions for development in the human body. Such animals as rats, dogs, cats, and various domestic animals must very often be exposed to infection with human parasites, yet they habitually harbor very few of them.

Many parasites must reach their ultimate destination in the body of a host by circuitous migration. In normal hosts a series of influences or stimuli guide them in the right direction, and they only occasionally get lost. In strange hosts these road signs are misleading or missing, and the parasites become aimless wanderers in abnormal situations, unable to find their way to the localities in the body where they can successfully mature. Human hookworms, for instance, are guided by some condition in a human being to enter lymph or blood vessels in the skin, and so eventually reach the lungs and then the intestine; *Ancylostoma brasiliense* does likewise in its normal hosts but fails in man, and rambles in the skin, causing creeping eruption. Species of

Gastrophilus, the horse bots, find their way to the digestive tract of horses, but in man the guiding influences are missing and they creep about under the skin. *Paragonimus*, gnathostomes, and *Lagocheilascaris* are other worms which lose their way in the human host and end up in cysts in places where they have no business. The larvae of the pork tapeworm encyst in the muscles of the normal pig host, but in man they often blunder into the eye or brain.

Spread to New Hosts. All animals tend gradually to extend their range by adapting themselves to slightly different conditions. Parasites, however, are at a disadvantage as compared with free-living animals, for while a song sparrow can find an infinite number of intergrading conditions between the damp, cool forests of the northwest and the dry, hot deserts of the southwest, an *Ascaris* can find no intergrading conditions between the conditions in the intestine of a pig and those in the intestine of a human being. The change must be made in a single jump or not at all.

The closeness of the bond between parasites and their hosts varies greatly; some parasites, e.g., *Trypanosoma cruzi*, are very indiscriminate; others, like *Taenia saginata*, are limited to a single species. Some genera and even species have maintained their allegiance to particular hosts or their descendants through vast periods of time. One species of tapeworm, for instance, is parasitic in ostriches in Africa and rheas in South America, but in no other birds. Parasites often give true clues to phylogenetic relationships, as a number of writers have shown [e.g., Cameron (1952), Rothschild and Clay (1952)]. By their parasites ye shall know them!

Parasites, having a less changeable environment than their hosts, tend to evolve more slowly, so that while a host is differentiating into species, genera, families, or even orders, the parasites in the host may change relatively little. The result may be that in related or sometimes unrelated hosts we may have parasites physiologically adapted to these different hosts and not easily transferable to others, yet showing only average differences in morphological characters, if any at all. Such, for example, are *Ascaris* in man and pig, dwarf tapeworms in man, mouse, and rat, and the itch-mites, *Trichomonas*, etc., of a variety of hosts. Some parasitologists are inclined to consider very closely related parasites in different hosts as distinct species until proved otherwise, whereas others tend to lump them all together. It seems to the writer preferable to regard them as hostal varieties or races which can be referred to as *Sarcoptes scabiei* of horses, man, etc., for instance, rather than giving them definite species or subspecies names about which troublesome questions of priority, identity, etc., are sure to arise. Much

the same situation exists for geographical races or subspecies of free-living organisms. There are many instances among parasites where a particular strain of a parasite is somewhat better adapted to one host than to another, but *can* be adapted to a new host. As yet there is no sound evidence to show whether this is due to selection of the fittest of random genetic types, to mutation induced by a changed environment, or to somatic adaptation.

The Names of Parasites

In all branches of natural history it has been found not only expedient but also necessary to employ scientific names, for there are estimated to be more than 10 million species of animals. Common names, like nicknames, vary from place to place, and often the same name is applied to quite different organisms in different places. Linnaeus, in the eighteenth century, devised a system of "binomial names" which consisted of the genus name, beginning with a capital letter, followed by a species name, in zoology beginning with a small letter, and both Latinized in form, since Latin came nearer to being a universal language than any other. Strictly, the genus and species names are followed by the name of the man who first gave the species name, in parentheses if the genus name is not the one he originally used, but in ordinary references to species this is omitted. The genus name may be likened to a surname and the species name to a given name, e.g., *Ascaris lumbricoides* is comparable to Smith, John.

Family names in zoology always have the ending "idae" attached to the root of the type genus, e.g., Muscidae from *Musca*, Ascarididae from *Ascaris* (root ascarid); superfamily names end in "oidea," but there is no standard ending for orders or classes. In botany the family ending is "aceae," e.g., Spirochaetaceae.

In order to avoid confusion there were adopted (in 1904) rules of nomenclature, known as the International Code of Zoological Nomenclature, which makes it impossible for any two animals to have the same name. A genus name can apply to only one genus in the entire animal kingdom, and a species name to only one species within a genus. The tenth edition of Linnaeus' *Systema Naturae* (1758) is accepted as the starting point for the names, no name proposed prior to that time having any standing. The first valid name given an animal is considered the correct one. Of course, if an animal is put in the wrong genus, it must be transferred to the right one. If a genus is split up, the animal may have to be placed in a new genus; for example, the old genus *Oxyuris* has been split into a number of genera. *Oxyuris equi* of the horse was the earliest one placed in the genus, therefore the

restricted genus *Oxyuris* must contain this species and any others which fall into its subdivision of the old genus; since the human oxyuris falls into a different subdivision it comes out with the next available genus name, *Enterobius*. For the same reasons *Filaria bancrofti* is now *Wuchereria bancrofti*, etc. If two genera are combined, the older genus name applies to all the members of the merged genera. If the same animal is given different species names by different workers, the earliest name applies.

Although this system was established to prevent confusion, in many instances strict application of the rules has resulted in just the opposite. The number of possible errors and misinterpretations are disheartening, in consequence of which names, long recognized and accepted, have to be discarded for others, because someone shows that the established name was really first applied to another species, or an earlier name was overlooked, or for some other reason. Unfortunately, the commoner animals are the ones which suffer most, for they are the most likely to have been redescribed by various workers and to have been shifted about from genus to genus. Unfortunate as this situation is, it is better than having no rules at all, and steps are now being taken to make names which have been in common usage for many years inviolable. The synonymy, or list of aliases, of some of our common parasites is already deplorably long. In some instances there is a difference of opinion as to what the correct name should be.

Although the scientific names are sometimes barbarously long and at first may be very annoying and even terrifying, every student of parasitology, as of every other branch of biology, must overcome any childish aversion he may have for them, and become used to accepting and using them. They are not obstacles to be avoided, but valuable tools without which there would be hopeless confusion.

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Part I PROTOZOA

• 3 •

Introduction to Protozoa

Place of Protozoa in the Animal Kingdom. It is usual for zoologists to divide the entire animal kingdom into two great subkingdoms, the Protozoa and the Metazoa. These groups are very unequal in number of species. The Metazoa include all the animals with which the majority of people are familiar, from the simple sponges and jelly-fishes, through the worms, mollusks, and the vast hordes of insects and their allies, to the highly organized vertebrate animals, including man himself. The Protozoa, on the other hand, are with few exceptions microscopic or almost microscopic animals, whose very existence is unknown to the average lay person. There is no question but that in point of numbers of individuals the Protozoa exceed the other animals, millions to one; a pint jar of stagnant water may contain many millions of these minute animals. Over 15,000 species of Protozoa have been described, but it is probable that there are thousands more which are not yet known to science.

Although Protozoa are usually considered to be fundamentally different from Metazoa by being unicellular instead of multicellular, the distinction is not as sharp as it would at first appear; some Protozoa form multinucleated plasmodial masses suggestive of syncytial tissues in Metazoa, and some colonial forms not only have somatic and reproductive cells differentiated from each other, but the colonies can also move and respond as units, and exhibit some degree of differentiation of anterior and posterior ends. The difference between such Protozoa and the simpler Metazoa is merely one of degree. Besides, although some complex Protozoa are not divided into cells, they have a greater variety of structurally different parts than some of the Metazoa (Fig. 1). For this reason some biologists prefer to think of the Protozoa as non-cellular organisms rather than as single-celled ones, since the latter designation suggests that they are to be compared with individual cells of a metazoan body.

The distinctions between Protozoa and other primitive organisms that exist as single cells or simple colonies is even more difficult, for there are transitional forms which link them to bacteria, fungi, and algae. In general they differ from bacteria in having distinct membrane-bound nuclei and in exhibiting sexual phenomena and often complicated life cycles, but there are a few Protozoa which have the nucleus broken up into many parts that are little more than granules, and some in which no sexual processes have been observed. Besides, even bacteria have been suspected of having sex, although on somewhat shaky grounds. Chemical reactions, staining properties, and the like are sometimes resorted to as distinguishing characters, but on these bases the spirochetes should be aligned with the Protozoa. Nevertheless, these organisms have now quite generally been abandoned to a botanical fate.

The slime molds, which the protozoologists call Mycetozoa and include with the Sarcodina, are also claimed by the botanists, who put them in with the fungi and call them Myxomycetes. The Sarcosporidia and *Rhinosporidium* are other organisms which were once claimed as Protozoa but have now been ceded to the mycologists; even *Toxoplasma*, an important parasite of man and animals, has recently been suspected of being related to the molds instead of the Protozoa.

Even more confusing is the case of the green flagellates, which protozoologists put in a subclass of the Mastigophora while botanists include them among the green algae. As Hall (1953) remarked, this suggests that protozoologists are unable to distinguish between animals and plants, which is disconcerting to those who like their taxonomy simple and consistent. To remedy this situation Calkins (1933) ejected the entire group of chlorophyll-bearing flagellates (Phytomastigophorea) from their relatives among the Protozoa. Some of the non-chlorophyll-bearing forms, obviously close cousins which had secondarily lost their chlorophyll, were arbitrarily transferred to Zoomastigophorea and thus retained in the Protozoa, but this kin-splitting didn't make anybody very happy.

The principal difference between plants and animals, when we get down to these primitive forms, is in their manner of nutrition. Plants synthesize their organic compounds from simple inorganic substances like CO_2 , H_2O , and nitrates, with the aid of chlorophyll, whereas animals utilize ready-made organic compounds or break down more complex ones and reassemble the parts to suit their needs. But according to this criterion a green flagellate (or alga!) like *Euglena* can be, and is, a plant by day and an animal by night. It is clear that between the higher plants and higher animals there is a broad no-man's

land of single-celled organisms which might be segregated into a buffer state, for which the name Protista was suggested by Ernst Haeckel many years ago. The boundary between Protista and Metazoa is fairly sharply defined, but that between the Protista and the lowest forms of Metaphyta (algae and fungi) is much more arbitrary.

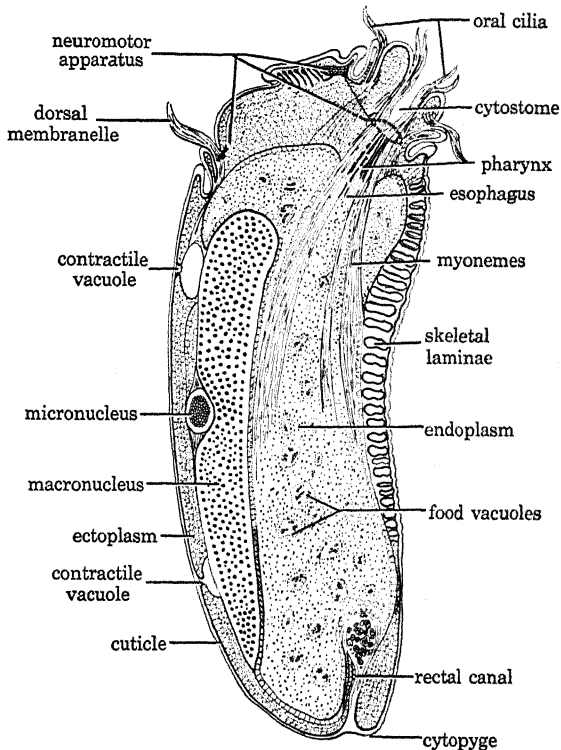


FIG. 1. A complex ciliate, *Diplodinium ecaudatum*, showing highly developed organelles. (After Sharp, Univ. Calif. Publ. Zool., 13, 1914.)

Structure. A protozoan, in its simplest form, conforms to the usual definition of a cell: a bit of cytoplasm containing one or more nuclei. In most Protozoa, even though in some cases there may be a number of nuclei present, these are all of one kind, but in the ciliates, except the primitive opalinids that inhabit the rectum of Amphibia, there are two quite distinct types of nuclei, a macronucleus filled with densely staining granules, and a micronucleus which is vesicular in structure, more like the nuclei of other Protozoa (Fig. 1); sometimes there may be a number of one or both kinds. In many Protozoa, e.g., the intestinal amebas, there is an endosome near the center, and in some of

these there are deep-staining granules encrusted on the inner surface of the nuclear membrane (Figs. 12, 13). The endosome may or may not contain chromatin; the chromosomes may form out of a zone of minute granules between the endosome and the nuclear membrane.

In most but not all cases division of the nucleus is accomplished by some form of mitosis or a process at least hinting at it; there is, however, no uniformity in the process as there is in Metazoa. Nature seems to have been experimenting with nuclear division in the Protozoa. Typical chromosomes are formed in some Protozoa, e.g., many amebas, but often there is no clear evidence of them. In *Entamoeba* mitosis takes place entirely within the nuclear membrane; a characteristic feature is the division of a *centriole* in the endosome into two, which migrate to opposite ends of the intranuclear spindle, but remain connected by a deep-staining strand called an *intradosome* until division of the six or eight chromosomes is completed. In the ciliates the macro- and micronuclei are formed, after sexual reproduction, from a single micronucleus.

The body of some of the simpler flagellates and amebas has no true cortex or pellicle, although the outer layer of the cytoplasm may be denser and less granular, forming an *ectoplasm*, in contrast to the *endoplasm*. Most other Protozoa have some sort of pellicle or cortex, giving them more or less definite shape. In ciliates the cortex is thick and contains a variety of structures (Fig. 1). Many Protozoa, particularly Sarcodina, produce shells of cellulose, chitin, cemented sand grains, silica, lime, or other substances, and some flagellates and ciliates have transparent chitinous loricas or tests, sometimes with collars (Fig. 2E).

Organelles. The term *organelle* is used in place of organ for structures that are only parts of a single cell. The organelles contained in a protozoan's body may be many and varied. Those connected with movement or locomotion differ in different groups. The simplest type of movement is by means of simple outflowings of the body cytoplasm known as *pseudopodia* (Fig. 2A). These are used both for locomotion and for the engulfing of food. In some species, e.g., the amebas, they are blunt, lobe-like projections of the body, but in others they are very slender and tapering, and in the Foraminifera they branch and anastomose into complex food-trapping networks. Some pseudopodia are permanently supported by axial rods, and these are called *axopodia* (Fig. 2B). Pseudopodia are the characteristic organs of locomotion of the entire class Sarcodina, to which the amebas belong, but many flagellates and Sporozoa, e.g., the malaria parasites, also have the power of ameboid movement by means of pseudopodia.

Flagella and *cilia* are usually constant in arrangement and form. Flagella (Fig. 2C) are characteristic of the class Mastigophora, but they also occur in some stages in the life cycle of certain amebas and in the sperm-like microgametes of Sporozoa. They are long whip-like outgrowths, capable of violent lashing or of rippling movements, and are composed of a fine filament, the *axoneme*, surrounded by a thin film of cytoplasm. The majority of species have only one or two flagella,

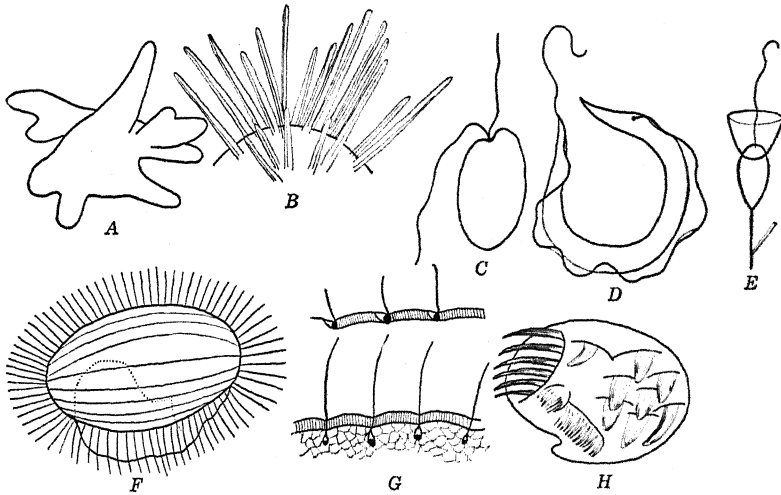


FIG. 2. Types of organs of locomotion in Protozoa: A, *Amoeba* with pseudopodia; B, a heliozoan with axopodia; C, *Bodo*, with two free flagella; D, *Trypanosoma* with flagellum attached to undulating membrane; E, choanoflagellate with flagellum and collar; F, *Pleuronema* with cilia and membranelle formed of fused cilia; G, modes of insertion of cilia; H, *Aspidisca* with cirri. (Figures F to H adapted from Calkins, *Biology of the Protozoa*.)

although many parasitic forms may have up to eight, but in some of the parasites (or symbionts) of termites and wood-roaches there may be hundreds. The flagella may be directed forward or trail behind, or may be attached to the side of the body by a delicate *undulating membrane* (Fig. 2D); if more than one is present they all may be alike, and perform similar functions, or they may be widely different.

A flagellum always arises from a minute deep-staining body called a *basal granule* or *blepharoplast* (Fig. 33). In many parasitic flagellates there is another deep-staining body called the *parabasal*. In the trypanosomes and their allies a similar body is called a kinetoplast (Fig. 26); it differs in being Feulgen-positive, therefore containing deoxyribonucleic acid, an essential ingredient of chromatin. In some Protozoa the blepharoplast is connected with the nucleus by a fiber

called a rhizoplast. The kinetoplast may also be connected with the blepharoplast by a fibril or even by a cone of fibrils (Fig. 33). Some flagellates have other specialized organelles connected with the blepharoplast, e.g., the *costa*, extending along the base of the undulating membrane in trichomonads, and one or more *axostyles*, varying from delicate filaments to a stout rod, also found in trichomonads as well as in some other flagellates, and acting as supporting rods (Fig. 19).

Cilia (Fig. 2F), which are characteristic only of the subphylum Ciliophora, have a structure similar to flagella, and like them arise from individual basal granules (Fig. 2G), but they are much shorter, more numerous, and beat rhythmically by a bending to one side. Cilia have much more coordination of movement than flagella, and regular waves of beats of the cilia can be seen passing over the body of a ciliate. The cilia may be fairly evenly distributed over the body in rows or may be in patches, and there are usually enlarged or specialized cilia, or membranelles formed of fused cilia, in the peristomal or other regions (Fig. 2F). In some creeping forms there are tufts of cilia fused together into stout organs called cirri (Fig. 2H).

Many Protozoa possess delicate contractile fibrils called *myonemes* (Fig. 1) which run in various directions in the ectoplasm or pellicle of the animal. In some flagellates and ciliates fibrils and minute deep-staining bodies have been described and have been interpreted as a more or less highly organized *neuromotor apparatus*, i.e., a definitely arranged and organized substance having a nervous control over the myonemes and cilia or flagella.

Organelles for food-taking occur chiefly in the flagellates and ciliates. Such Protozoa may have a *cytostome* or cell mouth for the ingestion of food (Fig. 1) and a *cytopyge* or cell anus for the elimination of waste matter. They may also have a delicate membranous *pharynx* and *esophagus* for leading the food material into the endoplasm, and *food vacuoles* into which the food is accumulated and in which it is circulated inside the body. In some protozoans, namely the Suctoria, a much modified group of ciliates, there are developed sucking tentacles for the absorption of food. In others there are tiny capsules in the ectoplasm, the *trichocysts*, containing minute threads which can be shot forth when stimulated, and used either for overpowering prey or for protection from enemies.

Protozoa, particularly those living in fresh water or soil, usually have one or more contractile vacuoles (Fig. 1). These are little cavities in the cytoplasm in which water collects, and which periodically contract, forcing their contents to the outside of the cell, sometimes through definite excretory pores on the pellicle. Their primary function seems

to be as hydrostatic regulators, to get rid of water which enters the denser cytoplasm of the organisms by osmosis. To a minor degree these act as excretory organs for elimination of metabolic wastes, but the many parasitic and marine Protozoa which lack contractile vacuoles, not needing them as osmotic regulators, seem to suffer no inconvenience; they get rid of their metabolic wastes through the body wall quite satisfactorily. The presence of a contractile vacuole is one feature by which free-living amebas in feces can be distinguished from true inhabitants of the intestine.

Sense organs in the form of pigment spots sensitive to light and processes sensitive to chemical substances, giving, perhaps, a sensation comparable to taste, are present in some free-living species.

Although no protozoan possesses all these organelles, many possess a considerable number of them and exhibit a degree of complexity and organization almost incredible in a single-celled animal which is barely, if at all, visible to the naked eye.

Physiology and Reproduction. In their physiology and manner of life the Protozoa differ among themselves almost as much as do the Metazoa. Some ingest solid food through a cytostome or wrap themselves around the food; others possess chlorophyll and are nourished in a typical plant manner, and still others absorb nutriment by osmosis from the fluids or tissues in which they live. Ingested food particles are surrounded by fluid, forming *food vacuoles* (Fig. 1), which circulate in the endoplasm. In ciliates they follow a regular course. Digestive fluids appear to be secreted into the vacuoles, and the vacuoles develop an acid reaction during digestion, later becoming neutral again. Undoubtedly the substances that can be digested vary widely with different Protozoa. Some species, e.g., *Entamoeba histolytica*, excrete substances which dissolve blood corpuscles and tissue cells outside the body, the soluble product being then absorbed through the body wall. Indigestible residue from solid food is extruded through the body wall; in forms having a pellicle this takes place through a cytopyge. Reserve food material is stored as glycogen, fats, oils, and other substances. Many parasitic forms store food in the form of *volutin* or *metachromatic granules*, which stain like chromatin. When preparing to encyst, some amebas form *chromatoid bodies* (Figs. 12 and 13) which contain reserve protein material.

Most free-living Protozoa are aerobic, using free oxygen in their respiration, but some, like certain bacteria, are anaerobic. Among parasites the respiration is sometimes aerobic and sometimes anaerobic, or it may be aerobic *or* anaerobic, according to the availability of oxygen.

The malaria parasites, leishmanias, and some trypanosomes (e.g.,

T. cruzi) have aerobic respiration, with a cytochrome system comparable with that in higher organisms, whereas trypanosomes of the *brucei* group, spirochetes, and such parasites as *Trichomonas vaginalis* and the intestinal amebas are strongly anaerobic in their metabolism. Instead of depending on oxidation for energy, they depend on dehydrogenation.

The multiplication or reproduction of Protozoa is of two quite distinct types, an asexual multiplication, more or less comparable with the multiplication of cells in a metazoan body, and sexual reproduction, comparable with a similar phenomenon in the higher animals. Several common asexual methods of multiplication occur amongst protozoans, namely, *simple fission*, or division into two more or less equal parts; *budding*, or separation of one or more small parts from the parent cell; and multiple fission or *schizogony*, which results from multiple or repeated division of the nucleus before the cytoplasm divides, thus producing a whole brood of offspring. In the flagellates simple fission is longitudinal, usually beginning with the blepharoplast, while in ciliates it is transverse. In flagellates the old flagella may be retained by one daughter, and new ones grow out from the blepharoplasts for the other, or the old ones may disappear and new ones form. Multiplication occurs in encysted forms in some species but not in others.

Protozoa which are in the phase of asexual multiplication are called *trophozoites*, in contrast to *gametocytes* which give rise to sex cells, and to *cysts*, which do not grow or multiply, although, early in their formation, the nuclei may multiply. The trophozoites of the Sporozoa, which multiply by schizogony, are called *schizonts*, and the daughters resulting from multiple division are called *merozoites*. After the sexual process a different form of multiple fission occurs called *sporogony*, ending in the formation of *sporozoites*. Cells intermediate between the parent cells and the merozoites or sporozoites may be formed, and these are called agametoblasts and sporoblasts, respectively.

Multiplication by one of the asexual methods may go on with great vigor for a long time, but sooner or later some modification of the process occurs. In many Protozoa a process comparable to sexual reproduction in higher animals occurs. In the ciliates this takes place by *conjugation*, i.e., a temporary union of two individuals during which time a daughter nucleus of one enters the other and fuses with a daughter nucleus, and vice versa; at the end of the process the two individuals separate, each being now a fertilized cell. In many other Protozoa two individuals, the *gametes*, unite permanently and their nuclei fuse, a process which is known as syngamy. Sometimes the gametes are indistinguishable from ordinary asexually multiplying individuals,

whereas in other instances the gametes are cells produced by a special process of multiplication; the parent cell is then called a *gametocyte*. When there is no visible difference between the gametes, the process of fusion is called *isogamy*, whereas when the gametes differ in size, form, motility, etc., the process is called *anisogamy*. There are, however, all gradations between isogamy and a condition of anisogamy in which one gamete, the *macrogamete*, corresponds closely to an ovum, being large, immobile, and with a relatively large amount of cytoplasm charged with reserve food material, while the other, the *microgamete*, is relatively minute, is actively motile by means of flagella, and contains very little cytoplasm, being thus essentially similar to a spermatozoon. In many species of parasitic Protozoa, e.g., the malaria parasites, the sexual cycle takes place in an alternate host; in others, e.g., the Coccidia, it takes place outside the body of a host.

In many parasitic Protozoa, for example the parasitic amebas and the intestinal and blood flagellates, no sexual process has been observed with certainty, although Fairbairn and Culwick reported in 1946 what they interpreted as conjugation in trypanosomes. In those Protozoa which do not show true sexual reproduction, i.e., exchange of nuclear material between different individuals, resulting in mixing of hereditary characters and also in rejuvenation of the cells, it is likely that some process occurs which brings about the rejuvenation, even if not the exchange of hereditary characters. Protozoan cells tend to grow old after continued asexual multiplication and lose their youthful vitality and reproductive power, just as do the cells of a metazoan animal. However, some strains of Protozoa, under favorable conditions, certainly do not grow old very fast, for Woodruff kept a strain of *Paramecium* going for 25 years without conjugation, and there was reason to believe it could continue indefinitely. As a matter of fact there is evidence that conjugation may cause quite a shock to *Paramecium*; in inbred lines Jennings showed that it might be 100 per cent fatal. In the Metazoa certain cells, the germinal or sex cells, are set aside for reproduction. This apparently also occurs in some Protozoa, but in most of them it is probable that any cell may be a potential sex cell.

Encystment. A great many Protozoa, at some time in their life cycle, are able to form more or less impervious protective capsules around their bodies, enabling them to survive unfavorable environmental conditions such as desiccation, unfavorable temperatures, injurious chemicals, or lack of oxygen. This process is called *encystment*. It is by this means that many parasitic Protozoa are able to survive conditions outside the body and to pass through the inhospitable environment of the stomach to reach the intestine or other organs of new

hosts. Most parasitic Protozoa that are not transmitted by intermediate hosts resort to cyst formation to gain access to new hosts, though a few, e.g., *Trichomonas* and *Dientamoeba*, manage without this.

In many Protozoa of water and soil, encystment occurs as a reaction to desiccation, but in the parasitic amebas and flagellates it is a normal phase in the life cycle, cysts being formed even when conditions are entirely satisfactory for continued multiplication of trophozoites. Encystment and excystment may both occur in the same culture medium, but each is favored by certain chemical and physical characteristics of the environment.

In the Sporozoa cyst formation is associated with sexual reproduction, the zygotes (fertilized gametes) being enclosed in *oöcysts* in which the sporogonic multiplication occurs, ending in the formation of a few to thousands of *sporozoites*. The sporozoites may be free in the *oöcysts*, as in the Haemosporidia, to which the malaria parasites belong; they may be enclosed, singly or in groups, in capsules of their own called spores, as in the gregarines; or they may be enclosed in sporocysts inside the *oöcysts*, as in the Coccidia. Trophozoites of amebas, flagellates, or ciliates prepare to encyst by ceasing ingestion of food and extruding food residue, but they frequently store up considerable amounts of reserve food in the form of glycogen, volutin granules, or chromatoid masses. This is the precystic stage. Then the cyst wall forms, and in many species a multiplication of the nucleus ensues. Mature cysts of *Entamoeba coli*, for instance, have eight nuclei and those of *E. histolytica* have four, but in *Iodamoeba* cysts there is only one.

When an encysted organism arrives in a favorable environment it excysts and begins to multiply in the trophozoite stage. In some amebas there is a complicated series of nuclear divisions in the multinucleate individual that escapes from the cyst, before any unicellular amebas are set free.

Classification. It is little wonder that the varied assemblage of single-celled animals constituting the group Protozoa should be difficult to classify. Many undergo profound modifications in the course of their life cycles, and the entire life cycle must be considered in any scheme of classification.

For a long time it was customary to divide Protozoa into four classes: the Rhizopoda or ameba-like forms, the Mastigophora or flagellates, the Ciliata or ciliates, and the Sporozoa or spore-forming parasitic forms. Doflein, however, modified this by first splitting the entire phylum Protozoa into subphyla, the Plasmodroma and the Ciliophora, an arrangement that has been quite generally followed by protozoolo-

gists. For our purposes we shall adopt the classification used by Jahn and Jahn (1949) and by Hall (1953), using the uniform endings for zoological names which Pearse (1936) suggested: for phyla and subphyla, *a*; class, *ea*; subclass, *ia*; order, *ida*; suborder, *ina*; and as everywhere used, for family, *idae* (*aceae* in botany). These have not been uniformly adopted by zoologists, but the idea is a good one. Following is an outline of the classification; further classification of the subphyla Mastigophora and Sporozoa is given on pp. 111–112 and 180–181, respectively.

Subphylum I. Mastigophora. With flagella throughout most of the life cycle, and a definite pellicle usually covering body. Sexual reproduction, where known, by syngamy. Flagellates.

Class I. Phytomastigophorea. Majority with chromatophores containing chlorophyll. Plant-like flagellates, arranged in six orders, and including such well-known free-living forms as *Euglena* and dinoflagellates.

Class II. Zoomastigophorea. No chromatophores; store lipids and glycogen but no starch or paramylum, and with no cellulose membranes or tests. Arranged in five orders, including all the parasitic flagellates.

Subphylum II. Sarcodina. Possess pseudopodia throughout most of life cycle, but may have flagella at some stage. Body with very delicate pellicle or none, but many free-living forms with tests or shells.

Class I. Actinopodea. Floating or sessile free-living organisms with axopodia (see p. 34). Peripheral cytoplasm foamy in character. Includes Radiolaria and Heliozoa.

Class II. Rhizopodea. Pseudopodia of lobose, filar, or anastomosing network types, but never axopodia or foamy peripheral cytoplasm. Arranged in five orders, including slime molds, amebas, and Foraminifera.

Subphylum III. Sporozoa. Parasitic forms with complicated sexual and asexual phases of the life cycle, and without locomotor organs in the adult stage.

Class I. Telosporidea. Zygote undergoes multiple fission (sporogony), producing sporozoites which after entering a host become trophozoites (schizonts), which multiply by schizogony and eventually produce gametocytes, except in the Eugregarinida, in which the trophozoite eventually becomes a gametocyte. Arranged in three subclasses and six orders. Includes gregarines, Coccidia, Haemosporidia, etc.

Class II. Cnidosporidea. Zygotes give rise to one or more trophozoites, without sporogony. Trophozoites produce characteristic spores composed of several cells, including one or more polar capsules containing coiled filaments that can be shot out, and one or more *sporoplasms*, analogous to sporozoites of the Telosporidea. Arranged in four orders, containing many important parasites of fish (Myxosporida) and of invertebrates (Microsporida).

Class III. Acnidosporidea. Life cycle somewhat like Cnidosporidea, but spores without polar capsules. Formerly Sarcosporidia were included, but these now considered fungi. Includes Haplosporida, parasites of fishes and invertebrates.

Subphylum IV. Ciliophora. Possess cilia in some stage of the life cycle.

Class I. Ciliatea. Cilia or structures made from them (cirri, membranelles)

present throughout life cycle. Arranged in two subclasses: *Protociliatia*, with nuclei all alike and sexual reproduction by syngamy; and *Euciliatia*, with nuclei of two types, macronucleus and micronucleus, and sexual reproduction by conjugation.

Class II. Suctorea. Adults without cilia, but with suctorial tentacles. Larval forms produced by budding, have cilia for short period. Sexual reproduction by conjugation in most forms.

The subphylum Sarcodina includes mainly free-living forms inhabiting ocean, fresh water, and soils. Some marine forms, e.g., the Foraminifera, are instrumental in building up chalk deposits out of their shells, and are useful in distinguishing geological strata. Others, the Radiolaria, form vast deposits of "radiolarian ooze." Only a few are parasitic, and these are all typical amebas which produce pseudopodia from any part of the naked body.

The subphylum Mastigophora includes a vast assemblage of organisms called flagellates, many of which bridge the gap between plants and animals. Here again the majority of the included forms are free-living; many of them possess chlorophyll and live like typical plants. Others have cytostomes through which they ingest solid food as do animals, and still others absorb dissolved substances by osmosis through their cell walls. Some, like *Euglena*, physiologically may be plants in the daytime and animals by night. All the parasitic species are of animal nature, feeding either by ingestion or by osmosis. Formerly the spirochetes were associated with the flagellates because of a supposed relationship with the trypanosomes, but this idea has long since been exploded, and spirochetes are now placed in a group by themselves, associated with bacteria rather than Protozoa, though in some respects they show affinity to the latter.

The subphylum Sporozoa includes a varied assemblage of parasitic forms, the relationships of which are discussed at the beginning of Chapter 9. They include numerous important agents of disease not only for all sorts of vertebrates, but also for invertebrates. Man is seriously afflicted only by the malaria parasites, but domestic animals are attacked by a number of different types.

The subphylum Ciliophora includes the most highly organized Protozoa. In one subclass, *Protociliatia*, are placed the ciliates which have from two to several hundred nuclei all of one kind, and which reproduce by fusion of gametes, thus being intermediate between the other Protozoa and the higher ciliates with functionally distinct nuclei and sexual reproduction by conjugation. Nearly all the members of this group are inhabitants of the large intestine of frogs and toads and do not concern us here. Members of the subclass *Euciliatia* have the most

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complicated organization of any Protozoa. The majority are free-living forms found in abundance in foul water, hay infusions, etc., whence the name "Infusoria" sometimes applied to them. Many inhabit the rumen or intestines of herbivorous animals, but, since they prey on bacteria and debris and do not attack the host itself, they may be regarded as commensals rather than parasites. Some are even symbionts, since they digest cellulose and in other ways contribute to the nutrition of the host. A few are at least potentially true pathogenic parasites, e.g., *Balantidium* (see p. 129), which parasitizes man, monkeys, and pigs. Both *Balantidium* and the digestive tract ciliates of horses and ruminants belong to the order Spirotrichida.

The class Suctorea, which lose their cilia and acquire suckorial tentacles as adults, are for the most part free-living organisms attached to various objects in water, but a few are parasitic on ciliates, and one, *Allantosoma intestinalis*, is of interest as a parasite of ciliates in the cecum of horses.

Parasitism and Host Specificity. It is very likely that parasitism among the Protozoa arose in the beginning by the ingestion by animals of free-living forms. Some of these may be conceived of as having found conditions of life satisfactory in the digestive tracts of animals which devoured them; in the course of time such forms would become more and more perfectly adapted to the new environment, and eventually lose their power to live and reproduce in the outside world. Such parasitism would be expected to occur first in cold-blooded aquatic animals and subsequently to extend to warm-blooded land animals. It is significant that most of the common genera of intestinal Protozoa of man, e.g., *Entamoeba*, *Chilomastix*, *Trichomonas*, and *Giardia*, have representatives in the Amphibia, in some cases so closely similar to the human species as to have cast doubts on their specific distinctness.

Many of the blood Protozoa have undoubtedly arisen by a process only slightly more complicated. They first adapted themselves to the digestive tracts of invertebrates; in bloodsuckers they would then become adapted to living in the presence of the blood on which the invertebrates fed; having survived this probationary treatment, such parasites might then be capable, if inoculated into the blood stream or tissues of the vertebrates on which their invertebrate hosts habitually fed, of adapting themselves to life in this new environment, which had thus been approached in an indirect manner. There is little room for doubt that the leishmanias and trypanosomes of vertebrates arose in this manner.

The specificity of protozoan parasites for particular hosts is a much disputed question. The striking similarity between such parasites as the various amebas, *Trichomonas*, and *Chilomastix* in different species

of mammals, together with the fact that nearly all the species from man are transferable to rats and other animals, throws grave doubt on the idea of fairly strict specificity which has been advanced by some protozoologists. Some intestinal parasites seem to have progressed in evolution to the point where they can inhabit only one or a few closely related hosts, but many have not evolved beyond the stage of hostal varieties, i.e., mere races of a single species, for the time being especially adapted to a particular host species by virtue of having lived in that host for a long time, but capable of transfer to a different host under favorable circumstances. Blood and tissue parasites, in general, show more specificity than intestinal parasites, but even among these there is much variation. The human malaria parasites are strictly confined to human beings, but the malaria parasites of birds show much less specificity. *Trypanosoma cruzi* is an example of a blood and tissue parasite that can infect such widely different mammals as opossums, armadillos, bats, rodents, dogs, and man. The question of host specificity is important from an epidemiological standpoint, since it involves the question of the extent to which other animals may act as reservoirs for human parasites.

Protozoan vs. Bacterial Disease. The general course of the diseases caused by Protozoa is different in some respects from that of the majority of bacterial diseases. Most bacteria attract leucocytes and are attacked by them; when they invade the body there is an immediate sharp attack by the leucocytes, followed by mobilization of the larger phagocytic cells of the body. The battle usually continues unabated until either the host succumbs or the bacteria are completely destroyed, with not a survivor left. The waxy-coated acid-fast bacteria of tuberculosis and leprosy constitute an exception. After a preliminary struggle, a sort of truce is struck and the disease settles down to a comparatively mild, chronic state in which there is a balance of power between invader and host, each one, however, ready to take advantage of the slightest circumstance which tips the balance in its favor. This is essentially the course taken by most protozoan infections also. Often, after an initial flare-up, there may be no symptoms whatever for a time, but the parasites are still present, suppressed but not destroyed, and ready to stage an insurrection the moment the resistance of the host is weakened by other invasions, or by exhaustion, malnutrition, etc.

A good example of the difference between a protozoan and a typical bacterial infection can be seen in the nature and course of amebic as compared with bacillary dysentery, the former with no pus and of long duration, the latter with abundant pus and of short duration. The sur-

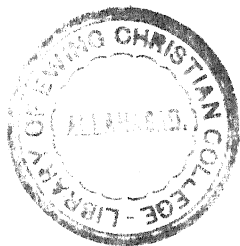
vival of protozoan infections in a chronic state seems to be due to immunity from attack by leucocytes, and the tendency of the other phagocytic cells of the body to relax their activity before their job is completed.

It is interesting, and perhaps suggestive, that spirochete diseases tend to be chronic like protozoan diseases, while the diseases caused by the rickettsias and by the insect-borne filtrable viruses (yellow fever, dengue, and sandfly fever) end in complete elimination of the parasites. In most bacterial diseases stimulation of the natural defenses of the host by means of vaccines or serums is more effective than it is in protozoan diseases. Chemotherapy by means of more or less specific drugs, e.g., iodine and arsenic compounds for amebiasis, antimony compounds for leishmaniasis, quinine and Chloroquine for blood stages of malaria, and 8-aminoquinolines for exoerythrocytic stages of malaria, is effective in most protozoan infections, whereas against bacteria no good chemotherapeutic drugs were known for a long time. Now, however, the sulfonamides and antibiotics have wide ranges of effectiveness against many types of bacteria. The effectiveness of antibiotics thus far known is far greater against bacteria than against Protozoa. It is interesting to note that even in their reaction to drugs, spirochetes are more or less in an intermediate position. Like Protozoa, they were long known to be specifically affected by a particular group of drugs (arsphenamines), yet, like bacteria, they are highly susceptible to antibiotics.

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• 4 •

Spirochetes

General Account. On the vague unsettled borderline between bacteria and Protozoa is a group of organisms, the spirochetes, some of which are waging a frightful war against human life and health. Some are free-living, some harmless commensals, some potentially pathogenic when the odds are weighted in their favor, and some are strictly parasitic and the cause of highly important human and animal diseases. Though long regarded as Protozoa allied to flagellates, they are now almost universally classed with bacteria. Most books in both protozoology and bacteriology discuss them, but in both they are usually passed over with less emphasis than they deserve. Until the bacteriologists are willing to assume full responsibility for them, it seems best that the protozoologists continue to give attention to this orphan group that Schaudinn left on their doorstep years ago, by confusing them with developmental stages of trypanosomes when he found them in an owl with a mixed infection.

Like bacteria, the spirochetes lack any distinct nucleus; their multiplication is by transverse division and is not longitudinal as in flagellates; they are not oriented into an anterior and posterior end; and the flexible cell wall or periplast is not like that of the Protozoa.

There are several different types of spirochetes. The true genus *Spirochaeta* (Fig. 3A) includes very long (200 to 500 μ) and relatively large organisms found in stagnant water, which have a central axis or filament around which the body is wound, like a piece of rubber tubing wound around a wire, as Wenyon expressed it. The genus *Saprosira* (Fig. 3B) contains large free-living forms with rather rigid undulating coils, forms found in both fresh and salt water, reaching about 100 μ in length. They are enclosed in a distinct periplast membrane, and have transverse septa dividing the body into chambers. There are no flagella and no "crista." The genus *Cristispira* (Fig. 3C) includes large forms (45 to 100 μ long) found in the crystalline style of mollusks. These also have a periplast membrane and septa. The body is thrown into

coarse spirals and has a flexible spiral membrane, the *crista*, appearing like a raised ridge along the concavity of the spirals.

The other spirochetes are relatively very small and slender, with flexible, spirally twisted bodies, like tiny corkscrews. Under an electron microscope they are seen to have a delicate cell wall or periplast, drawn out into a relatively coarse filament at one or both ends. The protoplasm contains scattered granules, and sometimes dense, irregularly spherical bodies are seen attached to the cells along the sides;

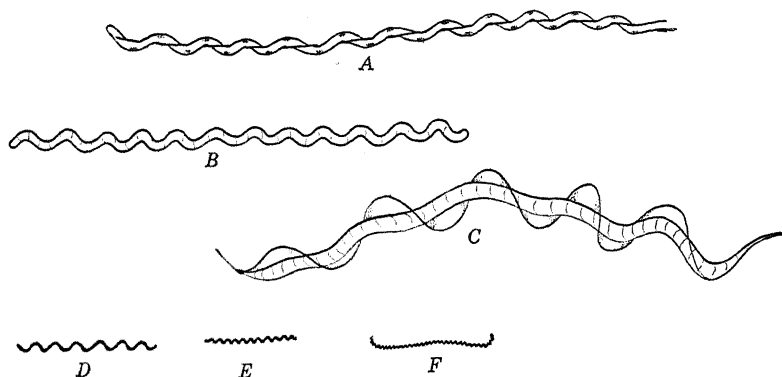


FIG. 3. Types of spirochetes, drawn to scale. A, *Spirochaeta plicatilis* ($500 \times 0.75 \mu$); B, *Saprospira grandis* ($50 \times 0.8 \mu$); C, *Cristispira anodontae* ($60 \times 1.8 \mu$); D, *Borrelia recurrentis* ($15 \times 0.25 \mu$); E, *Treponema pallidum* ($10 \times 0.25 \mu$); F, *Leptospira icterohaemorrhagiae* ($15 \times 0.2 \mu$). (Adapted from various authors.)

these have been interpreted as asexual spore-like bodies. Irregularly distributed flagella-like structures, single or in clusters, occur along the sides of the organisms (Fig. 4); some authors have interpreted these as fragmentations or shredding of the periplast. No granules or flagella-like structures are seen in *Leptospiras* (Fig. 11).

Spirochetes are very active in movement and dart swiftly back and forth across the field of a microscope, usually in straight lines if there are no obstructions. The movement is apparently by spiral wave motions passing through the body, though the possibility of flagella contributing to it must be considered. Spirochetes are also able to bend their bodies, and to oscillate while adhering to some object by one end.

Division of spirochetes is preceded by a fine drawing out of the periplast, like a glass tube drawn out after heating. Often two incompletely separated spirochetes twist about each other, giving the appearance of having split longitudinally. In healthy living spirochetes, when relaxed, the axis of the body is a straight line, but after being dried, as in blood films, the spirochetes may become distorted, and the actual

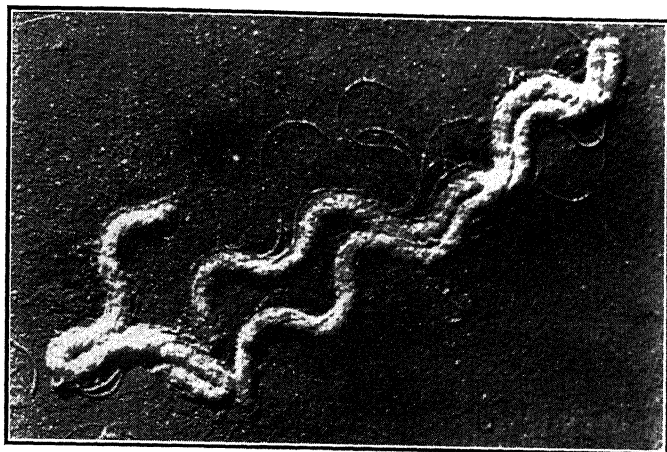


FIG. 4. Electromicrograph of *Borrelia vincenti*, showing "flagella." (From R. W. G. Wyckoff, *Electron Microscopy*, copyright 1949, Interscience Publishers, New York, London.)

spirals be obliterated (Fig. 5). A number of observers have described a breaking up of spirochetes into minute granules, and a subsequent growth of spirochetes from such granules, but the occurrence of this sort of phenomenon, though not impossible or even unlikely, has not been sufficiently confirmed.

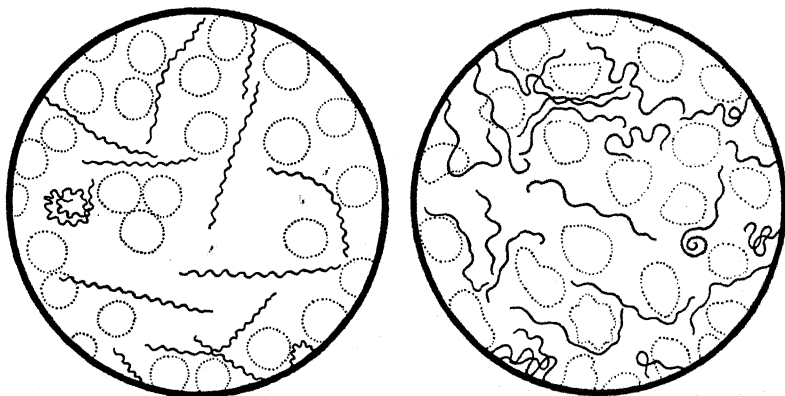


FIG. 5. *Borrelia duttoni*, showing appearance of spirochetes when living (left) and when dried and stained. $\times 1000$. (After Wenyon, *Protozoology*, London, 1926.)

The parasitic spirochetes fall into several natural groups, each of which has representatives found free-living in water as well as in the bodies of animals.

The first group, genus *Borrelia*, contains spirochetes with relatively large graceful coils (Fig. 3D); it includes the blood spirochetes that cause relapsing fever, and a number of saprophytic or pathogenic forms found in the mouth or other parts of the body, or in sores. The second group, genus *Treponema*, contains a few slender species with short kinky coils (Fig. 3E) and includes the spirochetes of yaws, syphilis, and pinta. The third group, genus *Leptospira* (Fig. 3F), includes excessively delicate forms in which the spiral rope-like windings are so minute as to be invisible in ordinary stained preparations, but visible under a dark-field or phase contrast microscope; these spirochetes show a few gross undulations of the body, which is usually bent hook-like at the ends. There has been no success in culturing pathogenic strains of either *Borrelia* or *Treponema*, but leptospires multiply readily in a variety of media containing serum.

The true spirochetes must be distinguished from the bacterial genus *Spirillum*, which contains organisms with rigid preformed spirals and with terminal flagella. The organism causing rat-bite fever, described by Japanese workers as *Spirochaeta morsus-muris*, was later shown to be a *Spirillum*.

The various species of spirochetes differ from one another in the length and coarseness of the body, in the number of spirals in a given length, and in the rounded or tapering form of the ends of the body. Many of the species described are indistinguishable morphologically, and are only recognizable by their pathogenic effects, places where found, immunological reactions, and methods of transmission. The relapsing-fever spirochetes, for instance, have been regarded by many workers as constituting many different species, separable on the basis of transmission by different species of ticks or by lice, cross-immunity tests between types, and pathogenicity for various laboratory animals. Likewise many different species have been described from normal and diseased conditions in the mouth, tonsils, lungs, intestine, skin ulcers, etc., which are not distinguishable morphologically. At present it is impossible to classify the species of spirochetes other than by their pathogenicity or otherwise, the types of infection produced, and the situations where they occur. The spirochetes of syphilis and yaws, for instance, cannot be distinguished with certainty from a form which occurs almost universally in normal mouths, on the tartar and about the roots of the teeth, and which is apparently perfectly harmless.

Spirochetes and Disease. Spirochetes are unquestionably responsible for several human diseases, among which are relapsing fever, syphilis, yaws, pinta, and infectious jaundice, and they are associated

with many other diseased conditions for which they are in part, or at times, responsible. The mere presence of spirochetes in sores or diseased tissue, however, is not sufficient reason for believing that they are the direct cause of the disease condition, for, like many bacteria, they are often found in exposed sores which are known to be due to other causes. Spirochetes are often found associated in sores or ulcers with various kinds of bacteria; in Vincent's angina a spirochete and a fusiform bacillus appear to be jointly guilty, the two living together in a sort of symbiotic relationship.

In general the diseases caused by spirochetes may be divided into four main groups. First, there is the febrile type of disease marked by a series of remissions and relapses, in which the spirochetes live and multiply mainly in the blood or lymphatics. To this group belong the various forms of relapsing fever, caused by species of *Borrelia*. Second, there is the type in which the spirochetes make a general invasion of the body and live primarily in the tissues, often localizing in particular tissues or organs after the preliminary general invasion, caused by species of *Treponema*. To this type belong syphilis, bejel, yaws, and pinta. Third, there are local infections or lesions in which spirochetes may be present in large numbers, and may or may not be the sole or primary cause. To this belong Vincent's angina, spirochetel bronchitis, tropical ulcers, ulcerating granuloma, etc., caused by *Borrelia vincentii* or related forms. Fourth, there are the *Leptospira* diseases, in which the spirochetes invade the body and eventually localize primarily in the liver and kidneys. To this belong infectious jaundice and a number of related infections found primarily in dogs, pigs, cattle, and rodents, which are transmissible to man.

Relapsing Fever

Some form of relapsing fever, caused by species or varieties of *Borrelia* multiplying in the blood, affects man in every continent in the world with the possible exception of Australia. Morphologically similar spirochetes occur extensively in other mammals and also in birds. The spirochetes that cause relapsing fever in birds, *B. anserina*, attack many different birds, and cause epidemics among domestic chickens, ducks, and pigeons; they are transmitted by ticks of the genus *Argas*. The mammalian strains, which are carried by ticks of the genus *Ornithodoros*, of which many have been named and described with various degrees of propriety, are capable of infecting a great variety of hosts. A single species or strain, e.g., *B. venezuelensis*, may be infective for opossums, armadillos, rodents, shrews, bats, carnivores, pigs, monkeys,

and man. Different strains, however, vary greatly in their pathogenicity for different hosts, producing anything from inapparent to rapidly fatal infections.

There can be little doubt that the relapsing fever spirochetes (*Borrelia*) were all primitively parasites of ticks of the family Argasidae, among which they are transovarially transmitted and can exist quite independently of any vertebrate hosts. Life in the blood of vertebrates must be considered a mere accidental occurrence, unfortunate as it sometimes is for the vertebrates. One strain of *Borrelia*, *B. recurrentis*, has become adapted to living in human lice (*Pediculus*), by which it is transmitted among human beings, producing great epidemics when conditions are favorable, such as during or after wars. This strain was undoubtedly originally derived from some argasid tick through the medium of human infections, but it is now so completely estranged from its ancestral hosts that it will no longer infect them. Along with its loss of infectivity for ticks this man-lice strain has lost its infectivity for other animals except monkeys and new-born rodents and rabbits. This *recurrentis* strain, however, has never become sufficiently adapted to its louse host to be transovarially transmitted by it, and thus to have become independent of a vertebrate host, in this instance man.

Tick-Borne Strains. As noted above, a great many strains of tick-borne spirochetes have been named. Great confusion exists concerning their classification which, as Baltazard (1954) pointed out, presents what may be an insoluble problem. Strains of the spirochetes apparently become biologically modified by life in different species or varieties of ticks, and perhaps to some extent in different vertebrates. Attempts have been made to separate them on the basis of staining reactions, cross-immunity tests, pathogenicity for various laboratory animals, and infectivity for different species of ticks. Of all these criteria the last is the most satisfactory, for as Davis showed in 1941 the spirochetes are very closely adapted to their particular tick hosts and are unable to infect any other ticks except sometimes by very transient infections, not sufficient to permit natural transmission. This would be a simple matter if it ended there; we could merely name the spirochetes after their tick hosts. But it *doesn't* end there. Baltazard showed that the spirochetes from ticks of the same species, e.g., *Ornithodoros erraticus* (small form), collected from various localities, even from different animal burrows in one locality, may show all degrees of refractoriness to infection of the same tick from other localities. Similar results were reported by Davis and Hoogstraal in 1954.

Only in central Africa is tick-borne relapsing fever primarily a human disease. This is because the vector, *Ornithodoros moubata*, has become

domestic, living in human habitations and feeding primarily on man. The spirochete involved, *B. duttoni*, is virulent for rats and mice as well as for man, but hardly at all for guinea pigs. In North Africa from Morocco to Tunis, and in Spain, a strain, *B. hispanica*, transmitted by *O. erraticus* (large form), causes sporadic human infections. The more widely distributed small form of this tick harbors spirochete strains, mentioned in the preceding paragraph, which differ from *B. hispanica* in being rarely if at all infective for man or adult guinea pigs, though it is very infective for small rodents and shrews. This complex of strains of spirochetes, according to Baltazard, should be called *B. crocidurae*. In the Middle East (Cyprus, Israel, Syria, Iran, Asia Minor) and Central Asia and northwest India another strain infective for man, *B. persica* (actually, like *B. crocidurae*, a complex), is transmitted by *O. tholozani*.

In the New World there are also a number of tick-borne strains. In Central America and northern South America a strain, *B. venezuelensis*, carried by *O. rudis*, fairly frequently infects man because its vector is carried into houses by rats. In California, Nevada, and the Northwest a strain carried by *O. hermsi* often makes life miserable for people vacationing in the high Sierras. During the winter the vacated cottages are inhabited by tick-infested chipmunks. Upon the return of the summer residents the chipmunks abandon their protected winter quarters and leave behind some of their ticks. These are often infected with spirochetes which are then transmitted to the vacationers, who come down with relapsing fever. Another strain, transmitted by *O. parkeri*, causes sporadic cases in wanderers in the northwestern woods. On the Mexican plateau human infection with a strain carried by *O. turicata* is fairly common since this tick has become semi-domestic there, and is frequently found in thatched huts, abattoirs and especially pigsties. In the United States, from Texas to Kansas, where this species of tick lives in caves and in burrows of animals, only sporadic human cases occur.

Louse-Borne Relapsing Fever. The louse-borne strain, *B. recurrentis*, is widely distributed in the Old World, having caused epidemics in many parts of Europe, particularly in the Balkans, Poland, and Russia; in North Africa, Egypt, Ethiopia, and Kenya in Africa; and in India, Indo-China, China, and Manchuria in Asia. After World War I a virulent louse-borne epidemic spread clear across Africa, south of the Sahara and north of the Equator, taking about 100,000 lives in ten years. The southward extension of the epidemic was limited by the absence of clothing on the Central African natives. Between World Wars I and II louse-borne relapsing fever practically disappeared from

southern Europe and North Africa, but fresh outbreaks occurred in the Balkans and North Africa in World War II.

There have been a few louse-borne epidemics in the United States and Mexico, but now the relapsing fever in the Western Hemisphere is all tick-borne.

B. recurrentis, as noted, has lost its ability to infect ticks, except in one case reported by Baltazard et al. in which the louse-borne strain became transmissible by *O. erraticus* after two passages through baby rodents. On the other hand, tick-borne strains have been shown to survive for some days and sometimes to multiply, in lice. Heisch and Garnham in 1948 succeeded in transmitting *B. duttoni* through four successive batches of lice, although the distinctive characteristics of true louse-borne strains failed to develop.

The Spirochetes. The spirochetes are usually 10 to 20 μ in length, averaging about 15 μ , and have a series of regular, graceful spiral turns of the body, each occupying 2 to 3 μ of the length. The ends of the body taper slightly. They may be extremely numerous in the blood, especially during the active phases of the disease, but they become very sparse, and often impossible to find, during the intermissions between relapses. When blood films are dried, the spirochetes become distorted and show irregular coarse spirals of quite a different nature from those present in the living organism (Fig. 5). During recovery from an infection, when antibodies are present in the blood, the spirochetes become immobilized and show degenerative changes, and are seen clumped together, with platelets and granules adhering to them. Some strains, at least, can be cultivated on artificial media, but often with difficulty. They can also be cultivated in developing chick embryos.

Immunological Strains. An interesting phenomenon is the immunological distinctness of the strains of the spirochetes which occur in the original infections and in relapses. Cunningham et al. (1934) showed that in the louse-borne disease, in which there is usually only one relapse, the onset and relapse strains consist of single antigenic varieties, one giving rise to the other, but in occasional second relapses a total of seven additional varieties were found. Schuhardt, (1942, *Pub. 18, Am. Assoc. Advancement Sci.*), showed that in the tick-borne *Borrelia turicatae* strain the spirochetes developing at onset or at relapses consist of multiple antigenic varieties, which undergo further alteration in rats as antibodies are developed against them. Schuhardt and Wilkerson (1951) showed that a single spirochete inoculated into a rat can produce a complete quota of antigenic variations in the course of the ensuing infection, and also that reversion to antigenic types produced earlier in an infection can occur. The spirochetes, in the course of an

infection, ultimately undergo all the variations of which that particular strain is capable. To what extent antigenic variations in spirochetes from different localities or vectors may differ or overlap has not yet been determined.

Life Cycle. There is still a difference of opinion as to whether the spirochetes have a granule stage, or even a filtrable stage, in their vertebrate or intermediate hosts; the data are conflicting, but the weight of evidence is swinging towards the nonoccurrence of any such stages.

When ingested by ticks the spirochetes persist in the stomach for 10 to 16 days, but within 6 hours some of them have penetrated into the body cavity. Ticks once infective probably remain so for life, and the infection is transmitted to the offspring through the eggs. It can also occasionally be transmitted by copulation. There is a considerable variation in ticks, both species and individuals, in their ability to pass their infections on to their offspring, but the infection can persist for many generations, possibly indefinitely, without need for a vertebrate host. The ticks themselves are the principal reservoirs. Transmission to vertebrates varies; it may be directly by bite, e.g., by *O. turicata*; by coxal fluid, e.g., by adult *O. moubata*; or perhaps sometimes by the feces. Nymphs of *O. moubata* often transmit by bite as well as coxal fluid, but adults only rarely have the salivary glands infected. *O. moubata* sometimes fails to infect by either coxal fluid or bite, whereas most species of *Ornithodoros* infect regularly.

In lice the spirochetes leave the stomach very quickly, and for some days the louse is negative for spirochetes and is non-infective, after which the organisms become numerous throughout the body cavity, and remain present and infective for the rest of the louse's life. Prenatal infections in man and animals have been known to occur.

Lice never transmit the infection by either their bites or their feces, but only when injured or crushed. In one case a man experimented upon in Algeria was bitten 30,000 to 40,000 times by gently handled infected lice without contracting the disease, but one louse crushed, and the body fluids brought in contact with the conjunctiva or a bite on the skin resulted in relapsing fever. Transovarial transmission by lice apparently does not occur.

The Disease. The most severe form of the disease is that of central Africa caused by *Borrelia duttoni*. The louse-borne types are usually milder, but their severity varies in different epidemics. The sporadic cases caused by *B. hispanica* around the Mediterranean and by *B. venezuelensis* in Central and South America are mild and usually occur in children. The various types of the disease differ in the number and duration of the relapses and intervening periods. After

an incubation period lasting about 3 to 10 days, the disease has an abrupt onset with nausea, headache, general pains, chills, and a rise of temperature, which lasts about 2 or 3 days in mild cases to 4 to 6 in severe ones. Then comes a crisis; the temperature falls rapidly to normal or below, and the patient recovers so rapidly and completely that he thinks it unnecessary to remain in the hospital any longer. Then, 4 to 8 days after the first crisis, comes a relapse, with a repetition of all the symptoms. A second crisis follows, and then a period of apparently normal health, which may be permanent or may be followed by more relapses. In general the louse-borne types have only one or two relapses, but some of the tick-borne types are likely to have four or five or even more, of shorter duration and more irregular in occurrence. The mortality is usually low, except in central Africa.

Immunity is of extremely variable duration, and sometimes more than one attack may occur within a year; but natives in endemic villages are usually immune, probably on account of repeated inoculations which keep up an immunity once developed. Immunity to one strain of the spirochete confers no immunity to other strains. Artificial immunity can be conferred, at least temporarily, by injections of killed cultures of mixed passage and relapse strains of the spirochetes.

Treatment and Prevention. Spirochetes in general, including those of relapsing fever, are susceptible to the effects of arsenic compounds, principally arsphenamines and Mapharsen (see p. 66), and to penicillin. Spirochetes in the blood and general visceral tissues are easily killed by either of these types of treatment, but the diseases tend to relapse because the spirochetes invade the central nervous system, particularly the brain, where they are ordinarily uninfluenced by peripherally injected drugs. After cessation of treatment, reinvasion of the blood and viscera may occur. Applied heat or fever induced by malaria not only directly affects spirochetes in the central nervous system but also enhances the action of drugs, presumably by favoring their penetration into the nervous tissues.

In the treatment of relapsing fever neither the arsenicals nor penicillin has proved reliable. Schuhardt and Hemphill in 1946 found that intraperitoneal injection of penicillin into mice with relapsing fever fails to kill the spirochetes in the brain. Moreover, they found that brain invasion practically always occurs, and within the first few days. That the brain spirochetes reinvading the blood stream are actually the cause of relapse seemed evident from the fact that mice given 1000 units of penicillin into the cranium, as well as an adequate dose into the peritoneum, failed to relapse. There is no doubt that penicillin is of real value in relieving symptoms of relapsing fever by

destroying the blood and tissue spirochetes, even though permanent cure may not result. Large doses over a long time might be effective; 200,000 units every 6 hours for 10 days was reported to be effective against a louse-borne strain in Korea. Recent work (Charmot et al., 1953), confirmed by Gefel and Rubenow in Israel, indicates that Terramycin is very effective since, although it does not readily pass the healthy meningeal barrier, it does so when this is damaged by infections.

Eradication of vermin from person and home and avoidance of places where infected parasites might be acquired are the most important protective measures in places where a louse-borne epidemic is raging. Methods for the control of ticks are discussed on p. 568, and of lice on pp. 611-612.

Treponematoses—Syphilis, Bejel, Yaws, and Pinta

Eight species of the slender, kinky-coiled spirochetes of the genus *Treponema* have been described and named. Four of them are pathogenic, and will not multiply in artificial culture media; these are *T. pallidum* of syphilis, *T. pertenue* of yaws, *T. herrejonii* (= *carateum*) of pinta, and *T. cuniculi* of a syphilis-like disease of rabbits. The others are saprophytic forms which thrive in the mouth or genitalia or (one species) in pond water; these can be cultivated, as can certain non-pathogenic strains, supposedly of *T. pallidum*, isolated from syphilitic lesions. Work by Eagle and Germuth (1948), however, suggest that these are probably really saprophytic contaminants of the syphilitic lesions; one was found to be serologically identical with a saprophyte drawn from the mouth. The treponemas are slow growers; some forms, at least, divide only at 30-hour intervals.

There has been unending discussion as to whether the human treponematoses are separate entities or manifestations of infection by the same parasite, modified by climate and race, and adapted to contagious or venereal transmission. The spirochetes of these several diseases are indistinguishable morphologically and are very much alike biologically; to some extent, at least, the diseases produce immunity to each other, though this seems not to be true of pinta and syphilis; and in general the diseases run a similar course, with early and late stages separated by a latent period. Hudson (1946) believes that there is only one pathogenic species, which, according to circumstances, can be propagated by either venereal or non-venereal routes. According to this view, treponematoses in the tropics retains its primitive character as a contagious or insect-transmitted skin disease of children, while in cooler and drier climates it changes to a venereal disease of adults.

That there is a close relationship between the spirochetes of syphilis, yaws, bejel, and pinta there can be no doubt, nor can there be any opposition to the idea that they have evolved from some common ancestor which probably, as Hudson suggests, had its origin as a tropical skin parasite. They are all antigenically similar, and respond to the same serological tests, and they also respond to treatment with arsenicals and penicillin, but these facts cannot logically be advanced as arguments for their identity.

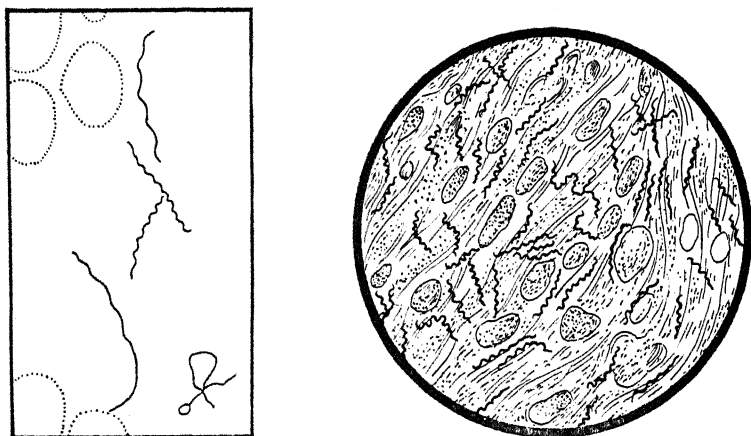


FIG. 6. Left, spirochetes from a syphilitic lesion. The two in the center are *Treponema pallidum*; the others a saprophyte, *T. refringens*. Right, *T. pallidum* in liver tissue of a syphilitic fetus.

Clinically the several diseases named show numerous differences; they have very different geographic distributions, and they differ in their modes of transmission. Whether one was originally evolved from another, or whether under suitable conditions the alteration can still occur, are largely academic questions. Practically, syphilis, yaws, and pinta are recognizably distinct diseases, and it is therefore reasonable to consider the spirochetes that cause them to be distinct. Perhaps they should be considered strains rather than species, but there would be no practical advantage in reducing the species names they have been given to the rank of varieties, and burdening the literature with longer names.

All these spirochetes (Fig. 6) vary in length from about 4 to 14 μ ; they usually have 6 to 14 very regular, short, sharp coils, each occupying about 1 μ . They are very active and dart rapidly across a slide, threading their way between cells or other objects in their way. The saprophytic mouth forms may be very abundant, along with *Borrelia*

and *Leptospira*, in some mouths, but scarce or absent in others. Cleanliness or healthiness of the mouth seems to have nothing to do with it.

SYPHILIS

History. Syphilis is one of the commonest, most insidious, and most deceptive diseases afflicting man in temperate parts of the world. Rosenau says, "civilization and syphilization have been close companions"; the one has followed in the wake of the other like the guerillas behind an army. Opinions differ as to the origin of syphilis among civilized nations. An oft-repeated but not widely accepted story is that it was acquired by Columbus' crew in Haiti and carried back to Spain by them, whence it rapidly spread all over Europe, causing an unusually intense outbreak of venereal disease.

The spirochete of syphilis, *T. pallidum*, was discovered by Schaudinn in 1905; a year later Wassermann discovered the serological test which, with much improvement, still bears his name and is still extensively used for diagnosis; in 1910 Ehrlich discovered an arsenical drug, Salvarsan, derivatives of which were the classical drugs for treatment of syphilis for nearly 35 years; and in 1943 Mahoney, Arnold, and Harris first demonstrated the miraculous efficacy of penicillin for treatment. The possibility today of curing the great majority of cases of syphilis by a single injection of a special penicillin preparation (see p. 66), in contrast to the 18-month regime of arsenical treatment that was formerly necessary, constitutes one of the most revolutionary developments in therapeutic progress, even in an age of such revolutions. The most recent important contribution is the *T. pallidum* immobilization (TPI) test for correct diagnosis of cases which seem to be falsely positive by serological tests. Today, with easy and dependable treatment, a more or less enlightened public, and progress by Public Health officials in case and contact finding, early diagnosis, etc., the outlook for the ultimate reduction of syphilis to a minor public health problem is indeed bright.

Prevalence. In spite of recent progress, syphilis is still a deplorably common disease, though nothing like what it was in the recent past. From 1933 to 1939 there were over 20,000 deaths ascribed to syphilis in the United States. This number has gradually decreased to about half in spite of greater accuracy in reporting. There has been a similar decrease in mental disease due to syphilis, and infant mortality from this cause has decreased by nearly 90 per cent. Congenital syphilis has shown quite as gratifying a decrease; about 13,000 a year are reported, and there are probably 100,000 undiscovered cases in children under 1 year to 10 years old. The total number of civilian syphilis cases is well under 200,000 and is steadily dropping. Over

half of these cases are in late stages of the disease. The annual incidence of reported new cases dropped to about 70,000 in 1951, about one-third of what it was in 1947. Of course, the actual number of cases is probably twice those reported, since many patients still rely for treatment on drugstores, quacks, or the grace of God.

Although the disease invades both the penthouse of the millionaire and the hovel of the tramp, all classes of society are not equally attacked. In general, the prevalence of syphilis increases as we descend in the social scale, and is more prevalent among Negroes in the United States, and these in the South, than among the white population. Since it is primarily a venereal disease, it is acquired most frequently between the ages of 15 and 30.

Distribution of Spirochetes in the Body. *Treponema pallidum* can readily be found in the primary stage of the disease; the organisms are abundant in the lymph under the raised rim of the initial sore or chancre and in enlarged neighboring lymph glands. During the second phase of the disease and also toward the end of the first phase, the spirochetes make a general invasion of the entire body but are not always readily found. They occur in variable numbers in the blood but may become abundant in "mucous patches" in the throat and sometimes in the skin. Very early they make their way into the cerebrospinal fluid of the brain and spinal cord; 80 per cent of syphilitics show evidence of invasion of the spinal fluid from the date of the primary sore, and are therefore possible candidates for syphilis of the nervous system.

During the latent period that follows the second phase the spirochetes are difficult if not impossible to find, even when the patient remains infective. In the tertiary stage the parasites usually show some special predilection for certain tissues or organs. The gummy sores or "gummas" which often break out during this third stage of the disease have usually been considered non-infective, but the parasites have been found in some of these lesions also. In congenital syphilis the parasites often multiply in enormous numbers in the unborn child, penetrating practically every organ and tissue of the body. The liver especially is often found literally teeming with spirochetes (Fig. 6, right).

Treponema pallidum in nature attacks only human beings, but monkeys and rabbits can be experimentally infected; the course of the disease in these animals is milder, and there are no lesions of the viscera or central nervous system. Mice can be infected in the brain, but show no symptoms at all; brain material from such mice is said to be infectious even when there are no demonstrable spirochetes.

Transmission. Syphilis, at least in temperate climates, is fundamentally a venereal disease, transmitted by sexual intercourse, and over

90 per cent of cases are undoubtedly of such origin. It is a common belief that this is the only way in which the disease can be acquired, and sometimes an unjust stigma is attached to an innocent case of syphilis. However, because of the delicacy of the spirochetes and their inability to survive more than a very brief time, usually a few minutes, outside the body, the disease is usually acquired only by intimate contact, such as sexual intercourse or kissing. It is closely associated with promiscuous sexual relations, but is often transmitted to a husband or wife, or from parents to children before or at birth, or by nursing.

Kissing is the commonest method of transmission next to sexual intercourse, since "mucous patches" swarming with spirochetes often develop in the throat during the secondary stage of the disease. An instance is on record where seven young women at a church social acquired syphilis from kissing a young man who had a syphilitic sore on his lip. Another case was traced to the eating of apples sold by an Italian who was in the habit of spitting on his fruits and rubbing them on his sleeve to shine them. This is the only instance known to the writer in which a venereal disease was transmitted by a food handler in line of duty, although many cities require evidence of freedom from venereal disease before providing health cards for food handlers. Unsanitary barbers and dentists sometimes spread infection, and dentists and physicians themselves may contract the disease by handling syphilitic patients, the spirochetes readily entering the smallest cut or abrasion of the skin. Midwives and wet nurses are likewise exposed to infection from diseased babies, as are the babies from diseased nurses. The fragility of the spirochetes and short life outside the body make transfer by towels, bed linen, eating utensils, or hands improbable.

The semen and vulval or vaginal secretions, as well as the throat, may be infective even when there are no visible lesions. In about 50 per cent of cases venereal contacts with infected individuals during the incubation period of the disease, before any lesions appear, are infective. Mothers with untreated primary or secondary syphilis almost always transmit the disease to a fetus between the fifth month of pregnancy and delivery, resulting in a pitifully high incidence of congenital syphilis. Forty states in the United States now have prenatal testing laws, which should have a good effect if enforced, for treatment is a perfect protection for the child as well as a cure for the mother. Enforcement of premarital serological tests for syphilis is also very helpful by reducing transmission from one spouse to the other.

Bejel. In the tropics where yaws is common, syphilis is uncommon. However, in certain areas in Europe, the Middle East, and Africa where living standards are very low, there are non-venereal forms of syphilis,

sometimes distressingly prevalent especially among children (Guthe and Willcox, 1954). Hudson (1938) described this type of syphilis as practically universal among the Syrian Arabs, by whom it is called "bejel"; like yaws, it is a contagious disease of children, but differs strikingly from that disease in the frequency of oral mucous patches. The children, instead of prostitutes and their clients, serve as a reservoir. The difference in epidemiology is due to different levels of personal hygiene; when people live in squalid huts or caves in warm countries, half-starved, nearly naked, unwashed, huddled together when sleeping, eating from a single utensil, careless with excreta, and attacked by hordes of ectoparasites, the delicate spirochetes are easily transmitted by contagion, but a slight rise in hygienic level results in sexual intercourse alone supplying sufficiently intimate contact for the safe passage of the spirochetes, which are far more delicate than most bacteria. It is possible, however, that the spirochetes of bejel and related non-venereal forms of syphilis may represent distinct strains more or less intermediate between those of yaws and syphilis.

The Disease. Syphilis is a disease which has no equal in its deceptive nature, which largely accounts for the many tragedies resulting from its ravages. It may remain latent and unsuspected for twenty years or more, and the carrier may remain infective, or return to an infective state, for as long as five years. About 45 per cent of those who later become victims of general paralysis from syphilis never can have any children, either on account of sterility or repeated abortions. The only pity of it is that this is not always true, for those who are brought into the world are often hopelessly handicapped either mentally or physically. About 15 per cent of blindness is due to syphilis and mental disease is very common. There is some reason for believing that the hideous, mentally deficient children known as mongols are the result of syphilis in parents. And finally, the carrier of latent syphilis may later develop general paralysis or some other disease of the nervous system, heart disease, or other conditions, which will render him an ineffectual social unit, and make him and his family a burden to the community.

The spirochetes are believed to be able to penetrate any mucous membrane, and will go through even a microscopic abrasion in the skin. Once under the surface they multiply rapidly and migrate by way of the lymph glands and then, within 12 hours, spread over the entire body. For this reason application of chemical prophylactics after exposure is progressively less reliable after the first hour or two.

In the majority of cases the disease begins with a small hard sore on the skin or mucous membrane known as the "primary chancre"

(Fig. 7). This usually appears at the point of infection in 10 days to 6 weeks, usually about 4 weeks, after the infection occurs. It has raised edges with reddish serum-encrusted center, and feels like a movable cartilaginous button. Although nearly always present except in congenital syphilis and in pregnant women, it is frequently inconspicuous and is easily overlooked. In non-pregnant women it may be located on the cervix or more rarely in the vagina, where it is difficult to find; it is also difficult to find when it is in the mouth. The chancre is most frequent on the genital organs, but may appear on lips, tongue, fingers, or other parts of the body. It is believed to be an allergic reaction.

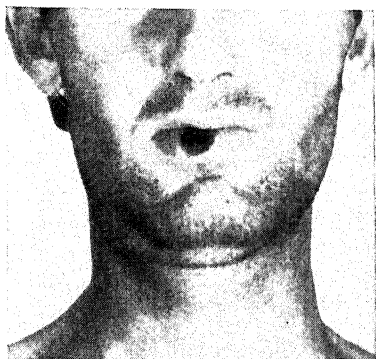


FIG. 7. Chancre on lip. (U. S. Army Institute of Pathology photograph 44845.)

The chancre gradually heals up and the second stage begins, in which constitutional symptoms appear, such as fever, anemia, and a general run-down condition. Often there is an extensive breaking out on the body, production of scaly patches of skin, an inflammation of the mucous membranes of the mouth and throat. Headache, rheumatic pains, and enlarged glands are common.

Following the secondary stage there is usually a latent period lasting several months to many years, usually 2 to 3 years, before the deeper lesions become prominent. Often there is a revival of the secondary symptoms before the appearance of the tertiary ones.

From this point on the course of the disease depends on what particular tissues or organs the spirochetes especially attack, for although the parasites, as said before, may produce disease almost anywhere in the body, in any given case there is usually a localization. It seems that certain strains of the parasites have special preference for certain tissues. The differences in this respect have been shown by Nichols to hold good through many transfers from animal to animal, and visible differences in the parasites have been claimed. In about 40 per cent of cases in temperate climates syphilis settles in the nervous system, causing a great variety of evil effects, such as mental disturbances, tabes or locomotor ataxia, general paralysis, epilepsy, insanity, and moral defectiveness. During 1945 there were nearly 75,000 hospital admissions in the United States for psychoses due to syphilis. Among tropical natives, on the other hand, neurosyphilis is practically unknown;

it has been suggested that this may be due to malaria or other fevers, which have been shown to have curative effects on syphilis of the central nervous system.

Another very common and even more fatal localization is in the aorta or heart. It is often not diagnosed until too late; it is responsible for one third of all fatal cases of syphilis. This cardiovascular form of the disease has not decreased as much as other forms of the disease in recent years, and so its relative prevalence is greater. Syphilis of the skin or mucous membranes often produced gummas, once thought to be the usual tertiary stage of the disease. Syphilis may select the bones, muscles, reproductive system, or any other part of the body, in each case producing a different set of symptoms. A form of "malignant syphilis" occurs in adults in which ulcerating sores appear early and gradually eat away large portions of the skin. Unborn babies are not subject to such specialized attacks as are adults, but they often have all the organs and tissues in the body invaded by the spirochetes.

An active attack on one tissue or organ of the body seems to have an inhibiting effect on other attacks and therefore usually prevents reinfection. Treatment of skin syphilis is sometimes followed by a flare-up of the disease in the nervous system, where the spirochetes were not destroyed by the treatment; on the other hand, paralytics with an active attack on the central nervous system seldom shows any other symptoms.

It is an odd fact that pregnancy tends to suppress or prevent the effects of syphilis; often the first suspicion of a conceptional infection is a miscarriage or premature stillbirth of a syphilitic fetus. Even the fetus is protected for 3 months; miscarriages earlier than that are not due to syphilis, and no evidence of fetal syphilis can be found short of 4 months. Beck and Daily suggest that the protection may be due to the corpus luteum hormone. It is presumably because of the protective effect of pregnancy that the incidence of serious late manifestations of syphilis is far more frequent in men than in women. Pregnancy may actually be helpful in the treatment of late syphilis. It is because of the frequent lack of symptoms that positive Wassermann reactions during pregnancy have often been considered false.

Diagnosis. The modern methods of diagnosing syphilitic infection have revolutionized our knowledge of the disease and have done much toward placing its treatment and control on a scientific basis. In at least 50 per cent of late syphilitic cases no symptoms can be attributed positively to syphilis, but we now have tests which make it possible to detect syphilis in practically any phase. In the chancre stage, examination of expressed serum for spirochetes, under a dark-field microscope, is very reliable and much better than any of the staining methods;

of the latter the Fontana stain is the best. Often spirochetes can be demonstrated, on a dark field, in material obtained from puncture of an enlarged lymph gland.

A few weeks later, and invariably during the secondary stage, syphilis causes a "reagin" to appear in the blood which can be detected by a number of serological methods, comparable with the tests for specific antibodies in other diseases. The reagin is non-specific only in the sense that it does not react with the spirochetes causing the disease, but with lipoidal extracts from animal tissues; extract of beef heart is used in the tests. Recent investigations indicate that the reaction is due to a breakdown of host tissues by the spirochetes and release of tissue lipoidal substances (haptenes), which combine with the spirochete protein to form a complete antigen, stimulating antibodies that react with the lipoidal tissue extracts commonly used as antigen in serological tests for spirochetal diseases. False positive reactions may be due to release of similar substances by tissue breakdown from other causes, and formation of the whole antigen by combination with other proteins. It is clear that these tests have no relation to antibodies developed against the spirochetes themselves, and therefore no relation to true immunity. Perhaps that is why the serological reactions often become very weak in old chronic cases, when the immunity is presumably highest.

The serological tests are based on the detection of the reagin, in the presence of the lipoidal extracts of tissue used as antigen, by either a complement fixation or a precipitin test. The former is known as the Wassermann reaction; the Kolmer and VDRL (Venereal Disease Regional Laboratory) techniques are commonly-used standardizations of it. If reagin is present it combines with the antigen and fixes the complement, otherwise the complement is still free. To determine whether or not the complement has been fixed, a suspension of red corpuscles and specific antibodies for the corpuscles, called hemolytic amboceptor, is added. If the complement is still present, as it should be if the tested serum is not syphilitic, the sensitized corpuscles are dissolved; whereas if the complement has been fixed, showing the presence of reagin and therefore syphilis, the corpuscles remain intact.

The most widely used precipitation test is the Kahn test, but other valuable ones are the Kline and Hinton tests. Any of these tests require skill, care, and good judgment in their performance; they are by no means foolproof. In expert hands there are very few false positives, but the tests are not as sensitive as they should be; only 65 to 90 per cent of known syphilitic cases are detected. Unfortunately, in public and private laboratories the results are not always so good. In any

case the serological findings should be very carefully checked if they do not fit with clinical observations.

In cases of neurosyphilis the spinal fluid also usually contains reagin, sometimes even when the blood does not, and should be tested. In babies born of syphilitic mothers serological tests are not always reliable during the first month or two, and examination of scrapings of the umbilical cord for spirochetes is desirable.

Although not infallible, the serological tests for syphilis constitute one of the most valuable and dependable means of diagnosis known in medicine. With a little further standardization, and improvement in the care and skill of technicians, their value will be still further enhanced.

An important recent development is the *Treponema pallidum* immobilization test (TPI) worked out by Nelson and Mayer (1949). *T. pallidum* obtained from testicular lesions of rabbits within 7 to 14 days after inoculation, before there is time for much antibody reaction, are freed from the tissue, suspended in a special medium in which they will live for several weeks, and tested for immobilization in the patient's serum plus complement. It is an expensive, complex, and cumbersome technique, but valuable for interpretation of serological tests that may be falsely positive. It would be enormously simplified if a method for artificial cultivation of the spirochetes could be developed, as for leptospiras.

Treatment. No development in the history of treatment of disease has been as spectacular and far-reaching in its effect as the development of penicillin treatment of syphilis. In the 1930's the course of treatment recommended for early and secondary syphilis was weekly injections of arsphenamines and bismuth for 18 long months. If the treatment began in the chancre stage and was never interrupted, about 85 per cent of the patients were cured. In the early 1940's efforts were made to speed the treatment by continuous intravenous drip of Mapharsen for 5 days, or by multiple injections for 6 to 8 weeks. A fair number of patients were cured, but an uncomfortable number of them died. For late syphilis, particularly of the nervous system, even 18 months of treatment aided by heat treatments provided by "hot boxes" or inoculated malaria failed in a deplorable number of cases.

In 1943 penicillin was shown by Mahoney, Arnold, and Harris to be highly effective against syphilis, but it originally involved numerous injections at 2- to 3-hour intervals for a number of days. Today a form of penicillin (PAM) is available which is slowly absorbed over a period of several days; it is procaine penicillin G in oil, gelled with 2 per cent aluminum monostearate. One injection of 2,400,000 units cures about 90 per cent or more of cases in the primary or secondary

stage, practically 100 per cent in the incubation stage. Even in neurosyphilis the majority of cases respond to administration of 600,000 units daily for 6 consecutive days. Arsenic and bismuth appear to be unnecessary as adjuncts, and fever likewise, except possibly in occasional late serious manifestations which have proved refractory. Until irreparable damage has been done, penicillin is equally effective for cardiovascular cases. In all cases treatment should be followed up by clinical and serological observation at 2- to 4-week intervals for 6 to 12 months to catch the occasional cases that are not cured by one treatment.

Today it is no longer necessary for patients to go to special treatment centers for cure of syphilis. More and more private physicians are treating cases instead of sending them to the centers. Fortunately desensitization to penicillin is usually possible in patients who are allergic to it, and there is evidence that other antibiotics can be substituted. It is also fortunate that, contrary to what might have been expected, there is no evidence of the development of resistance to penicillin on the part of the treponemas.

Prevention. Since syphilis can easily be diagnosed as soon as it reaches an infective stage and can be rendered non-infectious by treatment, this disease is theoretically more amenable to control than many other communicable diseases. Yet in our own country it was allowed to continue its depredations with little effort to check it until recent years—since Parran, in 1936, gave it a “coming-out party” and succeeded in making the public more or less aware of its ravages; prior to that time even mention of it had been tabooed.

Control depends (1) on education of the general public concerning the prevalence and dangers of the disease, and the help afforded by diagnosis and treatment; (2) wider use of routine serological tests, e.g., compulsory premarital and prenatal tests, and tests on all hospital admissions and in every complete physical check-up; (3) careful follow-up of treated mothers and their children, and screening examinations of children at an early age; (4) easily available and free diagnostic service for all suspected cases; (5) adequate treatment, free to all who are unable or unwilling to pay for it; (6) enforced reporting of all cases, with follow-up of those delinquent in coming for check-ups after treatment, and greater vigor, accompanied by tact and know-how, in tracking down sources of infection and contacts, and in getting new cases to report promptly for treatment.

Case finding in early stages is of prime importance and can be done by investigation of contacts, education, or serological screening. Contact investigation is more effective with women than with men, whereas public education concerning symptoms, treatment, etc., is more effective

with men, partly because in women the initial lesion is not as easily observed and partly because women just do not want to "know for sure"—the same attitude that is frequently displayed towards cancer. Serological tests are, of course, less effective in finding early cases and thus reducing spread of the infection; they are valuable in reducing the backlog of old untreated cases and in the prevention of congenital syphilis. The most urgent need now is intensification of efforts to find early infectious cases, in order to prevent transmission; otherwise the problem of syphilis will be with us always. Unfortunately in this step there has been little improvement over the last years.

YAWS

Yaws or frambesia is a very prevalent disease, especially of children, in warm moist climates throughout the tropics, particularly in backward rural communities with low hygienic standards. It is believed to have been introduced into South America from Africa by the slave trade. The spirochete, *Treponema pertenue*, is morphologically indistinguishable from that of syphilis but produces somewhat different lesions in rabbits from those produced by *T. pallidum*. The fact that syphilis and yaws are never both prevalent in one locality is undoubtedly due to the reciprocal immunity conferred by these diseases on each other. In many places practically 100 per cent of the natives suffer from the disease in childhood.

After an incubation period of 3 or 4 weeks, with indefinite symptoms, a papule appears at the site of inoculation. This develops into a raspberry-like tumor which bleeds easily and has a dirty, yellow crust. This lesion is accompanied by malaise and aches and sometimes fever. Six weeks to 3 months later the secondary stage develops, beginning with a dry, hardened condition of the skin with scaling-off patches. In these there then develop secondary papules or yaws, so that the body may be covered with a whole crop of them (Fig. 8) which last for several weeks, with new ones appearing for a year or more. They are especially abundant on the face and in the axillar and perineal regions. When on the palms or soles the eruptions are very painful; they give the thickened skin a moth-eaten appearance and cause a peculiar gait, which gave rise to the name "crab yaws." As in syphilis, after a latent period tertiary lesions of skin, joints, or bones may occur, but the viscera, eyes, and nervous system seem usually to escape.

Yaws attacks the epidermis primarily, in contrast to the mesodermal predilections of syphilis. A disease known as gangosa, prevalent in many places in both the East and the West Indies and in Africa, causing a horrible ulceration of the entire nose and palate area, is believed to be

due to yaws; but this mucous-membrane involvement is due to direct spread from the skin in contrast to the primary mucous lesions in syphilis. Yaws is very seldom a fatal disease except in young children.

Transmission. Yaws is spread by contagion, often by either biting or non-biting flies, but the spirochetes always enter through some abrasion of the skin, such as ground itch from hookworm, leech or insect bites, scabies, vaccination wounds, and scratches.



FIG. 8. A case of yaws. (U. S. Army Institute of Pathology photograph.)

There is a considerable bulk of evidence incriminating eye flies (see p. 686) as vectors of the disease in various parts of the world, including the West Indies, Brazil, Assam, and Samoa. Workers in several West Indian islands have suspected *Hippelates flavipes* of being a prime factor in yaws transmission, and Kumm and Turner (1936) succeeded in transmitting the infection to rabbits by the bites of infected flies. It has also been shown that the spirochetes can successfully pass through houseflies.

Treatment and Prevention. Care of the general health of yaws patients and conditions leading to the free eruption of the yaws aid much in shortening and alleviating the course of the disease. Yaws responds even more readily than syphilis to penicillin. A single dose of 600,000 units of PAM (see p. 66) appears to be adequate for family or other contacts and for mass treatment. In late stages larger doses may be necessary. A number of other antibiotics have also proved effective against yaws. Like the spirochete of syphilis, *Trepo-*

nema pertenu shows no evidence of development of resistance to penicillin. Suppression of yaws depends mainly on isolating patients and giving prompt treatment to them and to people who have, or have had, contact with them.

PINTA (MAL-DE-PINTO)

Pinta, long thought to be caused by a fungus, was shown in 1938 to give positive Wassermann and Kahn reactions, and to be caused by a spirochete indistinguishable from those of syphilis and yaws. It is characterized by changes in the pigmentation of the skin, at first blue or slaty freckles or patches, later by complete loss of pigment on large spots or areas with deeper pigmentation in other places. In dark-skinned people, who are almost exclusively affected, it produces unsightly disfigurement. Sometimes, as in yaws, painful thickenings of the soles and palms occur; this is much commoner in Cuba than in Mexico. There are usually no subjective symptoms or any impairment of the general health, except sometimes in late stages when tertiary symptoms may appear, such as hypertension, heart lesions, and changes in the cerebrospinal fluid, as well as atrophy of the epidermis. The disease is not a cutaneous form of syphilis, since it can be inoculated into patients who have that disease in latent form.

It responds well to antisyphilitic drugs in early stages, but when loss of pigment is complete, the white spots are permanent. The spirochete was named *T. herrejoni* by Blanco, but was later named *T. carateum* by Brumpt, and this name has commonly, though probably erroneously, been used for it. It can easily be found in lymph from the affected areas. Infection is believed to be acquired by contact, but certain species of *Simulium* have been suspected as possible vectors.

This unsightly affliction is particularly common in southern Mexico, where there are estimated to be 270,000 cases, and in Colombia, but it is also found in Central America, Ecuador, Peru, and some West Indian Islands. In 1943 three cases were reported in the United States, where it is probably commoner than is supposed, since loss of pigment is sometimes ascribed to syphilis or to unknown causes. Loss of pigment also occurs in leprosy, but in that disease it is usually accompanied by loss of sensation.

Spirochetes in Local Infections

Saprophytic spirochetes of several types occur very commonly in the human mouth and sometimes in the intestine, genitals, or with *T. pallidum* in syphilitic lesions. Whether these apparently harmless

spirochetes are identical with the spirochetes which secondarily invade diseased tissues, and perhaps aggravate them, it is impossible to say.

Vincent's Disease, Tropical Ulcer, etc. One of the most important of these secondarily developing conditions is Vincent's disease, which appears to be caused by two entirely different organisms living in a symbiotic partnership, one a spirochete, which has been named



Fig. 9. A tropical ulcer. (U. S. Army Institute of Pathology photograph C43-1.)

Borrelia vincentii, and the other a large, cigar-shaped, fusiform bacillus. It affects either mucous membranes or subcutaneous tissue; in the mouth it causes "mal-de-boca" and "noma"; in the throat it usually follows a streptococcus infection and causes a diphtheria-like ulceration of the tonsils and throat known as Vincent's angina; in the skin of debilitated people it produces lesions called tropical ulcers or by the more impressive name, tropical sloughing phagedena (Fig. 9). A severe and very common form of the infection known as Naga sore occurs in Assam: the gangrenous process erodes tendons, muscles, and even bone, and a horrible, yellowish slough is formed which has a characteristic fetid odor. Ulcerations are not infrequent in the genital organs also. In Ethiopia noma is frequently fatal.

The organisms concerned are not primarily pathogenic, for they are

frequently found in healthy mouths and also about the genitals, and are often secondary invaders of various diseased tissues. Smith (1932) called them opportunists; only when normal health or resistance of tissues is lowered are they capable of invasion. That vitamin deficiencies may play a part is suggested by the response of the disease to relatively large amounts of niacin. The spirochetes are 12 to 25 μ long with six or seven loose coils to every 10 μ , and are always accompanied by the cigar-shaped bacilli, and often by spirilla and vibrios also.

Penicillin has a spectacular effect on Vincent's infections, and all lesions actually due to the spirochetes and the accompanying fusiform bacilli heal promptly with penicillin treatment, followed by good diet. Tropical ulcers can be healed by internal treatment with antibiotics as can other spirochete infections, or by local application of 3 per cent Aureomycin hydrochloride ointment repeated daily until healed. No spirochetes or fusiform bacilli are seen after 36 hours.

Bronchial Spirochetosis. Spirochetes sometimes become very abundant in the trachea and bronchial tubes, causing cough, blood-stained sputum, pain in the chest, and sometimes chronic pulmonary hemorrhages suggestive of tuberculosis. The spirochete is very variable in size and form. It has been named *Borrelia bronchialis*, but may be one of the mouth spirochetes invading tissue that for some reason has lost its normal resistance, or it may be *B. vincentii*, unaccompanied by the fusiform bacilli. Wenyon and some others are very skeptical of the pathogenic nature of the spirochetes; he thinks it would be as logical to consider every mouth abnormality as due to mouth spirochetes when these can be found there as to accuse the bronchial spirochetes of being the cause of the diverse pulmonary disorders in which they have been found present. The fact, however, that in acute uncomplicated cases immediate relief, accompanied by a disappearance of the spirochetes, has been effected by injections of arsphenamine and other spirocheticidal drugs is hard to explain if the spirochetes are mere saprophytic invaders without pathogenic power.

Leptospirosis

The delicate hooked-end spirochetes of the genus *Leptospira* are readily visible by dark-field or phase contrast microscope examination, but not by transmitted light. They stain with difficulty except by silver-impregnation methods, e.g., Fontana's stain, or with Giemsa's stain.

Some workers recognize no less than nineteen distinct strains of *Leptospira*, separable by antigenic differences, and most of them, if not all, capable of infecting man as well as the various animals which serve as reservoirs for them. One species, however, *L. biflexa*, is a sapro-

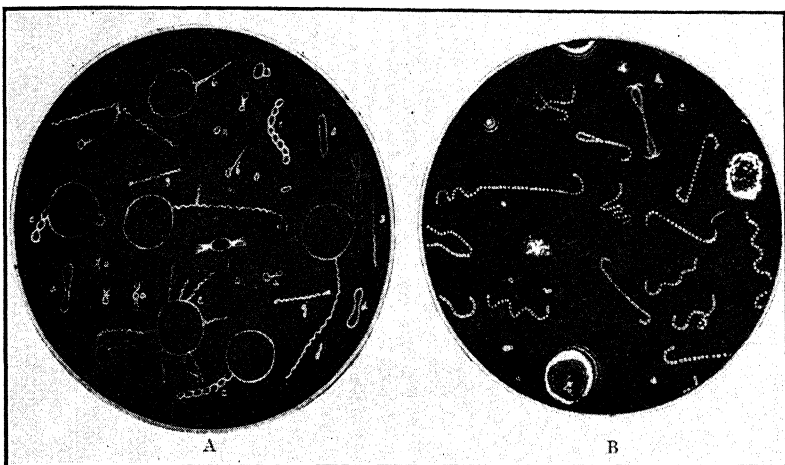


FIG. 10. *A*, *Leptospira*-like artefacts; *B*, true *Leptospira*; as seen by dark-field illumination. ($\times 1000$.) (*A*, after Knowles and Das Gupta, 1924. *B*, after Wenyon, from *Trop. Dis. Bull.*, 21: 282.)



FIG. 11. Electromicrograph of *Leptospira icterohaemorrhagiae* by Harry E. Morton. (From *J. Bacteriol.*, 45: 144, 1943.)

phytic water dweller. Attempts have been made to ascribe other than serological differences to these strains, e.g., pathogenicity for various animals, clinical symptoms produced, animal reservoirs, and geographical distribution, but only with confusing results (see van Thiel, 1946; Davis, 1948). A considerable degree of overlapping of antigenic types

occurs, i.e., the serum of an animal recovered from one strain reacts with other strains than the homologous one, though not at the same titer.

Human infections are most frequently acquired by swimming or wading in water or mud contaminated by urine or other excreta of rodents or domestic animals which serve as reservoir hosts. The organisms may survive in water for several weeks if it is not acid. Invasion of the body can take place through the mucous membranes, particularly those of the eye or nose, or through minute abrasions of the skin. In Germany the frequency of leptospirosis, caused by *L. icterohaemorrhagiae*, in people bathing in stagnant water has led to the name "slime fever," and in parts of Europe the disease caused by *L. grippotyphosa* in farmers working in marshes, especially during floods in late summer and fall, is called mud, swamp, or field fever; it has a reservoir in field mice. An outbreak of *L. pomona* infection in fifty of eighty young adults who had disported themselves in a swimming hole in an Alabama stream was linked with a prior outbreak in hogs, some which had succumbed having been found floating in the stream.

The clinical effects of leptospirosis vary greatly, even among cases caused by a single strain, although there are average differences between the effects of some of the strains. The severity ranges from rapidly fatal to inapparent infections. Usually there is sudden onset, after an incubation of 1 to 2 weeks, with chills, fever, headache, stiff neck, aches in the joints and muscles, vomiting, burning and intense injection of the eyes, and occasionally a rash. The fever lasts for about 7 to 10 days. In about 50 to 60 per cent of the cases of *L. icterohaemorrhagiae* infection (Weil's disease) jaundice develops; this was once considered so characteristic that the disease has been called "infectious jaundice." This symptom is less frequent, sometimes entirely absent, in some of the other leptospiroses. Meningeal symptoms develop usually in the second week, and may be the predominant feature, causing what is called aseptic meningitis. Another symptom is the bursting of capillaries or small blood vessels, causing hemorrhagic spots on the internal organs and mucous membranes, especially the eyes. Heart irregularities or even failure sometimes occurs, probably from direct invasion of the heart muscle by the spirochetes. Mortality varies from 4 to nearly 50 per cent.

Leptospirosis may be confused with typhus, from which it differs in not having the characteristic rash, and with yellow fever, dengue, or other virus infections, from which it can be distinguished by the presence of leucocytosis instead of leucopenia. Noguchi once isolated a *Leptospira* which he called *L. icteroides*, now known to be identical with the

Leptospira of Weil's disease, from cases of supposed yellow fever in South America, and thought he had found the cause of yellow fever.

The leptospiras can often be found in the blood the first day after onset of symptoms, and uniformly during the febrile period, but they disappear after 7 to 14 days. After about 10 days they appear in the urine and may persist in it for an indefinite time. The parasites ultimately become localized in the kidneys, where they may cause extensive damage. They may persist in a host for 2½ years.

Diagnosis may be made in early cases either by culture (one drop of blood to 5 cc. of medium), by inoculation of animals by blood or urine, especially guinea pigs, followed by blood culture in 4 to 6 days, or by a number of serological methods after 6 to 10 days.

Various agglutination tests or complement fixation can be carried out with formalin-killed cultured leptospiras, or living ones can be used for an immobilization test, which is also very useful for drug-testing. Low titers in serological tests are of no significance, but titers of 1/400 or over, or rapidly rising titers, are diagnostic. A titer may rise to 1/10,000 in the second week of the disease.

No entirely reliable treatment for the disease is known, aside from symptomatic care, although penicillin and other antibiotics have favorable effects and cure some cases. Treatment with polyvalent immune horse serum is helpful, but very large doses are needed, up to 60 cc. daily for 3 to 5 days—almost a transfusion!

Species or Strains. The commonest, most widespread, and longest-known *Leptospira* infection of man is Weil's disease or infectious jaundice, caused by *L. icterohaemorrhagiae*. This species is very common in the commensal brown rat, *Rattus norvegicus*, which is its most important reservoir. In Holland, Schüffner (1934) found an average of 45 per cent infected. Dogs are also susceptible. This *Leptospira* is found in all parts of the United States. Closely related serologically is *L. canicola* which commonly affects dogs in Europe and in the United States. It only occasionally affects man and rarely rodents; of common laboratory animals, only hamsters are susceptible. About 25 to 35 per cent of dogs in the United States show serological evidence of infection, and Coffin and Stubbs (1942) reported over 50 per cent mortality in some outbreaks. This disease is much more prone to cause uremia, and less frequently jaundice or hemorrhages.

L. pomona is a common infection of cattle, pigs, and horses in Europe, the United States, Australia, and the Orient; it also affects sheep. Bovine cases may be acutely fatal, with bloody urine, sometimes thick, bloody milk, and prominent meningeal symptoms. Anemia and emaciation occur in severe cases; jaundice may or may not be

present. In Israel bovine cases are caused by a different strain, *L. bovis*, which, like *L. canicola*, is not infective for most laboratory animals. Horses suffer mainly from iridocyclitis. In Switzerland and Austria human infections with *L. pomona* are known as "swineherd's disease." Meningeal symptoms are especially prominent in man, and this is also true of infections with *L. gryppotypophosa*, which, as noted on p. 74, has its reservoir in field mice. In Holland over 30 per cent of the meadow mice are infected with this organism.

L. gryppotypophosa, and also *L. autumnalis*, *L. ballum*, and *L. bataviae*, have all been found in the United States. *L. autumnalis*, known to produce virulent human infections in the Far East, has been incriminated as the cause of "Fort Bragg Fever" in the United States; this fever was once thought to be caused by a virus. *L. hebdomadis* causes a dengue-like disease called "7-day fever" in Japan, Malaya, and India; it is harbored by field mice. A common form of the disease in Java, in which jaundice is frequent, has been called pseudo-dengue, and is caused by *L. pyrogenes*. Two other Java strains, *L. bataviae* and *L. javanica*, are often acquired by cats, presumably from rats or mice. Still another rat strain, *L. australis*, was the cause of a human outbreak of the disease in Queensland in 1934; it was again found by Alicata in Samoa in 1949, and is believed by him to occur in Indonesia and Switzerland also. It runs a severe clinical course in man.

The distinctness of many of these strains may justifiably be doubted, and there is evidence that their immunological characteristics, which overlap somewhat, may be altered by cultivation and passage through animals.

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Amebas

Amebas are animated bits of naked protoplasm, familiar to every freshman biology student who peers through a microscope with appropriate marvelings at the simplicity of animal life in its most primitive state. The vast majority are free-living animals inhabiting soil, water, and decaying organic matter everywhere, and play an important role in the control of bacteria in some of these situations. In view of their wide adaptability and the frequent contamination of food or drinking water by their cysts, it is not surprising that some species of them have adapted themselves to living out the active phase of their lives in the intestines of animals. The majority even of these are harmless commensals, content to use the intestine as a haven of refuge where food is abundant and enemies scarce, but a few have developed a taste for live meat, and have taken to feeding upon the wall of the intestine that shelters them.

The amebas belong to the subphylum Sarcodina, class Rhizopodea, and order Amoebida (see p. 41). The members of this order are characterized by having lobe-like pseudopodia and no tests or shells. The species which live as commensals or parasites in the intestines of various animals, from termites and roaches to man, are placed in the family Endamoebidae; they are distinguished by having no flagellated stage and no contractile vacuoles. Recently a species morphologically indistinguishable from *Entamoeba** *histolytica* was found living in sewage.

Because of their small size, simple life cycles, and scarcity of good distinguishing characters, classification of Endamoebidae into genera and species requires a great deal of care and patience. Separation of Endamoebidae into genera is based on the character of the cysts and minute structural differences in the nuclei, and separation of species on still finer details of these characters.

Habits of Trophozoites. All the commensal and parasitic amebas, as far as known, inhabit the large intestine of their hosts, with the

* For use of "Entamoeba" vs. "Endamoeba," see p. 84.

exception of *Entamoeba gingivalis*, which makes itself at home in the mouth. *E. histolytica* and perhaps some of the others occasionally invade the lower part of the small intestine just above the ileocecal valve, and they can frequently be found in the appendix. They all multiply in the active or trophozoite phase by simple fission; in most species this is initiated by a division of the nucleus, but in one genus, *Dientamoeba*, the nuclear division usually occurs shortly after cell division, resulting in a high proportion of individuals with two nuclei. Most of the species are mere scavengers, feeding on bacteria, cysts, and various debris in the contents of the large intestine, but *E. histolytica*, and to some extent *E. gingivalis*, are more fastidious. Both have histolytic and cytolytic power, and undoubtedly feed in part on the juice of tissue cells which they dissolve. *E. gingivalis* occasionally picks up a bacterium or other types of food, but in its natural habitat in the mouth it lives mainly on leucocytes or their nuclei.

Encystment. Most of the parasitic amebas form cysts, which are better able to withstand conditions outside the body than are the trophozoites, but *Entamoeba gingivalis* and *Dientamoeba fragilis* manage to survive without them. When preparing to encyst, the amebas eliminate all food vacuoles, round up, and shrink somewhat, probably by a condensation of the cytoplasm, so that the nucleus becomes relatively large. This is the precystic stage. A delicate cyst wall develops to protect the organism during its hazardous existence outside the body while waiting for an opportunity to infect a new host. As long as the amebas are alive the cyst walls are relatively impervious to many substances, including dyes and weak disinfectants, but they have only feeble resistance to desiccation; *E. coli* cysts are more resistant than those of *E. histolytica*. The cysts are unaffected by either chlorine or dilute silver ions in the proportions used for killing bacteria in drinking water, but they are killed in a few minutes by 5 per cent acetic acid. The fact that living cysts are not ordinarily stained by dilute eosin, whereas dead cysts are, has been used extensively as a test of the viability of cysts in experimental work, but there is some question of its reliability. In some species glycogen is stored during encystment in more or less well-defined vacuoles, and there may be deep-staining "chromatoid bodies" containing reserve protein material. These gradually disappear as the cysts grow older.

In most of the species of amebas some multiplication of the nucleus takes place during the formation of the cysts, but in *Iodamoeba* the nucleus remains single. In *Entamoeba histolytica* and *Endolimax nana* four nuclei are normally produced, and in *Entamoeba coli* eight. The exact conditions which induce encystment are unknown. In most cul-

tures no encystment occurs in the absence of rice starch. It has been suggested that in cultures, at least, encystment is related to population growth, but whether to crowding or accumulation of waste products is unknown. The presence of bicarbonate plus various organic compounds, with a low oxygen tension, seems to be necessary for encystation in cultures. Cysts are not found in dysenteric or liquid stools and are never formed in tissues or liver abscesses. Encystment should be considered a naturally recurring phenomenon in the life cycle; its sole purpose is the safe transfer of the parasite from one host to another. A single cyst, at least of *E. coli*, may be sufficient to establish an infection (Rendtorff, 1954).

Excystment. The conditions which lead to excystment are also little understood, but most cysts "hatch" in the small intestine above where the trophozoites ultimately settle down. The amebas escape from their cysts through a perforation in the cyst wall. The process was first described by Dobell in 1928 for *Entamoeba histolytica*. The four-nucleated ameba draws itself in and out of the cyst several times before escaping. It then undergoes a complicated series of nuclear and cell divisions, resulting ultimately in eight little amebulas with a single nucleus each.

Species Found in Man. Prior to the appearance, in 1919, of Dobell's book, *Amoebae Living in Man*, the amebas found in man were in a terrible muddle, and most of the earlier literature cannot be relied upon as far as species are concerned. Since the publication of this valuable work there have been a number of suggested modifications or additions, but none of them has stood the test of time; today six species of amebas living in man are recognized and are separated into four genera, just as Dobell arranged them. All protozoologists recognize the following genera and species: *Entamoeba gingivalis*, inhabiting the mouth; *E. histolytica*, a pathogenic intestinal form; *E. coli*, *Endolimax nana*, and *Iodamoeba williamsi*, harmless intestinal forms except for one amazing case (see p. 103); and *Dientamoeba fragilis*, an intestinal form which is at least sometimes pathogenic.

There are two races of *E. histolytica* which differ in the size of their cysts, and also in their pathogenicity, the small-cyst race being almost if not entirely non-pathogenic to man, whereas the large-cyst race is a potentially pathogenic tissue invader. The small-cyst, non-pathogenic form has been considered worthy of recognition as a distinct species, *E. hartmanni*, by European workers, although American workers refer to it as "small-race *E. histolytica*." These races appear to breed true, although there is one record of a change from small to large cysts after 5 years in culture, but this observation needs confirmation.

Differentiation of Genera. The outstanding characteristics of the genera of amebas which occur in human beings are as follows:

Entamoeba. Nucleus vesicular with chromatin arranged in a peripheral layer of bead-like granules of fairly uniform size, and a small compact endosome; a capsule-like structure, can usually be seen surrounding the endosome. Cysts, if produced with 4 or 8 nuclei similar in structure to those of the free forms, and including also glycogen masses and refractile chromatoid bodies, though these masses and bodies commonly disappear before or soon after the cysts become mature. (See Figs. 12 and 13.)

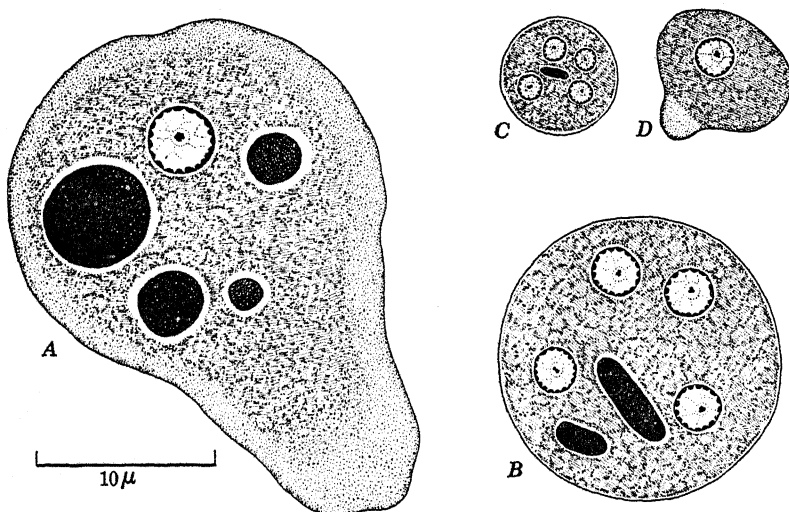


FIG. 12. *Entamoeba histolytica*: A and B, trophozoite and cyst of invasive, large-race form; C and D, trophozoite and cyst of lumen-dwelling, small-race form (*E. hartmanni* of European authors). $\times 2500$.

Endolimax. Nucleus vesicular without a distinct peripheral layer of chromatin. A fairly large compact endosome in the interior, usually more or less eccentric and connected by threads or processes with one or more smaller masses. Mature cysts oval, with 4 nuclei in the known species, similar in structure to those of the free forms. The cysts contain, in addition to the nuclei, a number of small refractile volutin granules. The young cysts also contain masses of glycogen. (See Fig. 14A and A'.)

Iodamoeba. Nucleus vesicular with moderate-sized central endosome and well-developed membrane without a distinct peripheral zone of chromatin, but with a single layer of rather large granules between the endosome and the outer membrane; cysts very characteristic, formerly known as iodine cysts or I cysts, of irregular shape, containing, besides a single nucleus, a number of brightly refractile granules and a relatively large, sharply defined solid mass of glycogen which stains deeply in iodine. The cyst nucleus is peculiar in that the endosome comes to lie peripherally in contact with the nuclear membrane. (See Fig. 14B and B'.)

Dientamoeba. Mature individuals with 2 similar nuclei; these are vesicular with the endosome represented by a cluster of small granules near the center;

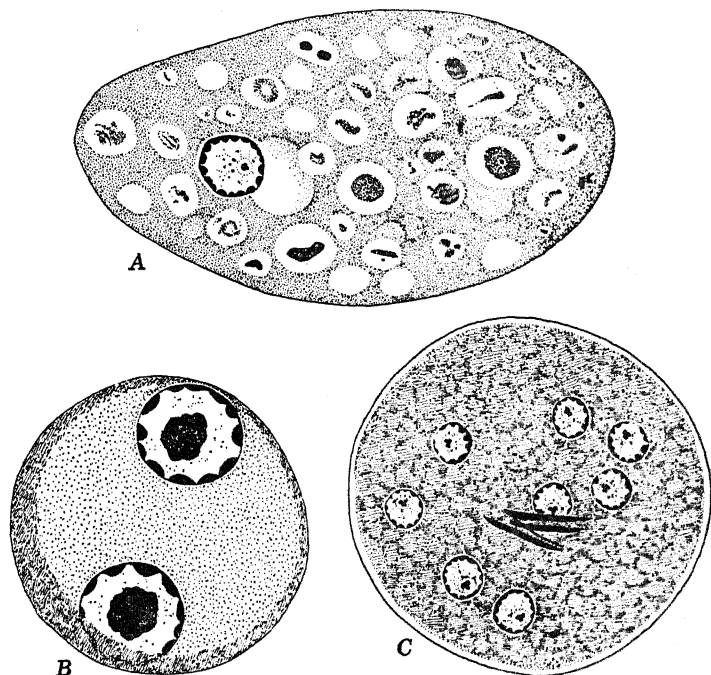


FIG. 13. *Entamoeba coli*: A, trophozoite; B, 2-nucleated cyst with large glycogen vacuole; C, young, mature cyst with splinter-like chromatoid bodies. $\times 2500$.

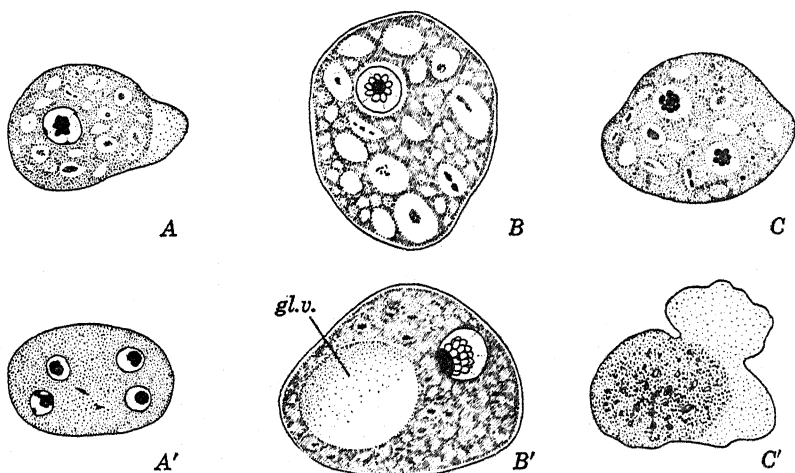


FIG. 14. A and A', *Endolimax nana*, trophozoite and cyst; B and B', *Iodamoeba bütschlii*, trophozoite and cyst, latter showing large glycogen vacuole (gl.v.); C and C', *Dientamoeba fragilis*, stained and living specimens, the latter with flat leaf-like pseudopodia. $\times 2500$.

nuclear membrane very delicate without distinct peripheral chromatin; trophozoites burst in water; cysts not found. (See Fig. 14C and C'.)

Host Specificity. There has been much discussion about the identity of the human species of amebas and morphologically identical ones found in other animals. Strict host specificity on the part of intestinal amebas can no longer be accepted, although some protozoologists have grimly adhered to belief in it in spite of growing evidence against it. The genus *Entamoeba* is an excellent one to illustrate the situation. In man there are two universally recognized intestinal species, *E. coli* and *E. histolytica*. The latter species can be successfully transferred to a variety of animals such as monkeys, rodents, rabbits, cats, dogs, and pigs. *E. coli* has been transferred to monkeys, cats, and rats. In various species of lower primates, from spider monkeys (*Ateles*) to apes, indistinguishable forms of one or both of these types of amebas have been described. Five of the species of human amebas (and four human flagellates) have been found by Kessel in *Macaca* monkeys, differing in no morphological or physiological respect from the corresponding Protozoa in man. Although these might have been acquired from contact with human beings, this is probably not true of forty-four wild Philippine monkeys, obtained where they probably had had no chance to be contaminated by their Protozoa-infested human compatriots, and which Hegner found to harbor eleven different species of human intestinal, oral, and vaginal protozoa. One was a veritable zoological garden for human Protozoa, harboring eight different species, and none had less than two.

Natural infections with *E. histolytica* occur in most of the animals in which experimental infections have been produced. Carnivorous animals, e.g., cats and dogs, rarely harbor amebas of any kind, whereas nearly all species of omnivorous and herbivorous animals harbor one or more species of their own as well as being susceptible to the human species. One species, *Entamoeba polecki*, common in pigs and various ruminants, occasionally infects man; it produces one-nucleated cysts. Reptiles harbor a number of species, including one, *E. invadens*, which is strikingly similar to *E. histolytica* and may cause fatal infections in lizards and snakes. Amebas belonging to the same genera as those found in man occur also in insects and other invertebrates. A species found in roaches, *Endamoeba blattae*, is thought by some to belong to the same genus as the species of *Entamoeba* in mammals; hence the name "*Endamoeba*" is often used, especially by American writers, but the correctness of "*Entamoeba*" is being more and more widely recognized. For a detailed discussion of this question see Kirby (*J. Parasitol.* 31: 177-188, 1945).

Cultivation. All the intestinal amebas, as well as the flagellates and ciliates (except *Giardia*), can be grown in artificial cultures, but most of them only in the presence of living "associates," of which bacteria, including many single species, *Trypanosoma cruzi*, and cultured tissue cells will suffice. A vast amount of effort has been put into a study of the growth requirements of amebas, especially *E. histolytica*, in an effort to develop an axenic (free of other organisms) culture medium. This has not yet been accomplished although Shaffer and Frye (see Shaffer et al., 1949) came near it with a preconditioned clear medium containing few bacteria.

Many media have been developed; some are entirely liquid (e.g., St. John, *Am. J. Trop. Med.*, 12: 1932; Balamuth, *Am. J. Clin. Pathol.* 16, 1946), and some are coagulated slants of whole egg, liver infusion agar, or serum, overlaid with various fluids, usually containing albumin or serum, and with rice starch added, on which amebas feed gluttonously. Some widely used media of this type are those of Boeck and Drbolav (*Am. J. Hyg.*, 5, 1925); Dobell and Laidlaw (*Parasitology*, 18, 1926); Cleveland and Sanders (*Science*, 72, 1930), now available as Difco's desiccated "Endamoeba medium"; E. C. Nelson (*Am. J. Trop. Med.*, 27, 1947), and various modifications of these.

The living associates mentioned above are required not just to help maintain a low oxygen-reduction potential for the amebas, as first thought, but also to provide, continuously, some needed intermediate product of metabolism. The amebas probably obtain this product by swallowing the organisms (or dissolving tissue cells). Dead associates do not constitute an acceptable diet, although non-mobile, slowly metabolizing ones suffice. In fact, better cultures are obtained if the bacteria are temporarily or incompletely inhibited by the addition of 150 to 500 units of penicillin G and 1000 units of streptomycin per milliliter of medium. In most media the amebas reach a population peak in about 2 to 3 days; transfers are made every 4 to 10 days, varying with the medium.

Coprozoic Amebas. Cysts of free-living amebas and flagellates, and sometimes even ciliates, may enter the body with food and pass through the alimentary canal unhatched and undigested. Some of these find conditions satisfactory for rapid multiplication in the feces after passage, and may confuse an unwary laboratory technician. All such amebas, however, are distinguishable by the presence of one or more contractile vacuoles. There is no evidence that these coprozoic forms can ever establish themselves and multiply in the intestines; they become progressively more abundant in stale feces, whereas the trophozoites of the true intestinal species die out very rapidly, usually within

a few hours after leaving the intestines. The discovery of an ameba in sewage, *Entamoeba moshkovskii* (see Neal, 1953), which can pass for *E. histolytica* even on close inspection, complicates diagnosis, for there is no reason to doubt that cysts of this organism may be swallowed under unsanitary conditions. That would make it necessary for a long-suffering technician, in order to make a positive identification of *E. histolytica* in asymptomatic cases, to culture the organism at 37°C. but not at 20° or below, since the parasitic species will not grow at the low temperatures but *E. moshkovskii* will.

Diagnosis. Diagnosis depends upon (1) finding the organisms in the feces and (2) making a correct identification of them. Cysts are rarely found in liquid or dysenteric stools, whereas trophozoites, except those of *Dientamoeba*, are less frequently found in formed stools. Cysts of intestinal amebas, and of other intestinal Protozoa also, are voided intermittently, so a single examination cannot be relied upon to bring to light all infections. When a series of examinations of a single group of people is made over a period of weeks, some parasites in the stools may show up regularly, whereas others appear and reappear without rhyme or reason, although there is no reason to doubt that the infection has been there throughout. The percentage of existing infections found at a single examination may vary from 20 per cent to 65 per cent, depending in part on the technique employed, time used, and skill and experience of the technician, but probably also on degrees of exposure and resistance of the people examined. In Egypt a single examination for 10 minutes by MIF reveals 50 to 65 per cent of existing infections with the three commonest species of amebas, when the incidences on six examinations were shown to be 97 to 98 per cent, whereas Sawitz and Faust (1942) found much lower percentages of actual infections revealed by a single examination in the United States. Better results are obtained by making examinations at intervals of several days than on successive days, and there is little advantage in examining several slides from the same stool.

Formed stools to be examined for cysts can be kept in the icebox for 2 or 3 days before examination, but trophozoites in liquid stools degenerate very rapidly unless preserved and should be searched for as soon as possible after being passed, while the stool is still warm. If the stools are kept at body temperature the trophozoites are usually still identifiable for about 30 minutes. A higher percentage of infections can be found in a single purged or diarrheic stool examined for trophozoites than in a single formed stool examined for cysts. Oil-purged stools are useless for examination.

Direct smear examinations are made by comminuting a small amount

of feces in saline, to which may be added 1:1000 aqueous eosin to stain the debris pink, leaving the living trophozoites and cysts unstained. After spreading the smear over the width of two cover glasses, apply a cover to one side for examination of living organisms; to the other side, before covering, add a small drop of D'Antoni's iodine (1.5 grams iodine in 100 cc. standardized potassium iodide, filtered after standing 4 days). The iodine will stain nuclei, chromatoid bodies, etc., well enough for identification. Additional aqueous instead of saline smears facilitate diagnosis by destroying fungus and *Blastocystis* and by showing certain characteristics of *Dientamoeba*.

An improved iodine-staining technique was described by Sapero et al. (1951). Brooke and Goldman (1949) showed that addition of fixative to 5 per cent elvanol, a polyvinyl alcohol, fixes and preserves trophozoites and small cysts very well, but large cysts are distorted. Smears so fixed can be dried on slides and subsequently stained without harm to the trophozoites. Sapero and Lawless (1953) described the MIF technique, by which specimens can be collected in the field, home, etc., and preserved in vials by unskilled workers. The specimens can be examined months later with the trophozoites and cysts excellently preserved and showing easily recognizable diagnostic characters.

Permanent, stained preparations showing minute details of structure can be made by fixing wet films with Schaudinn's fluid (equal parts of saturated HgCl_2 and 95 per cent alcohol) with or without polyvinyl alcohol; if the latter is used the films may subsequently be dried, otherwise not. These films are then stained with iron hematoxylin, in the use of which there are many variations (see Craig, 1944), all of them requiring skill, patience, and time. Lawless (1953) described a permanent-staining technique that requires no special training in its use and takes less than 3 minutes, which is very satisfactory for routine diagnosis. It should be noted that trophozoites are much more frequently found in MIF-stained preparations than in permanently stained slides, in which many are evidently lost.

Faust et al. (1939) worked out a method of concentrating both the cysts of Protozoa and eggs of worms by a zinc sulfate flotation technique. Saturated NaCl cannot be used for flotation, as it can for worm eggs, since it shrinks the cysts and makes them unrecognizable. The method is good only for cysts, but concentrates these to a considerable degree, after which they can still be stained (see pp. 255-256).

Other diagnostic methods are culturing, which some workers (Michael and Cooray, 1952) consider more accurate than fecal examination for intestinal infections; and complement fixation, which is particularly useful for amebiasis of the liver or other organs outside the

intestine, but which is often not positive in intestinal cases, especially if tissue invasion is slight (Hussey and Brown, 1950; Kenney, 1952; McDearman and Dunham, 1952). Norman and Brooke reported in 1954 that cultivation was an effective diagnostic technique for fresh purged stools, but not for stale normally passed specimens.

Entamoeba histolytica

Distribution and Incidence. Because of its capacity for causing disease, its wide geographical distribution, and its discomfoting frequency as a resident of the human colon, *Entamoeba histolytica* must be ranked as one of the most important human parasites. Although it once had the reputation of being mainly a tropical parasite, it is by no means so limited. It has world-wide distribution, and is almost as frequently present, though fortunately not so frequently pathogenic, in the land of apples and apoplexy as it is in the lands of mangoes and mañana. The only reason that this ameba often inhabits more people in tropical than in temperate localities is that the people in the tropics take less pains to avoid devouring its cysts with contaminated food or water. In the Kola Peninsula of Russia, lying entirely within the Arctic Circle, a 60 per cent incidence of *E. histolytica* was recorded.

When routine examinations are made by competent microscopists, seldom less than 5 to 10 per cent of the entire population, even in northern Europe and the United States, are found to be infected. In a state-wide survey of Tennessee, Meleney et al. in 1932 found more than 11 per cent of the rural population infected, and in one group of counties above 22 per cent; these findings on one examination indicate probably twice as great actual incidence. In one group of 27 individuals in 5 backward families, 23 were carriers of *E. histolytica*. The Chicago outbreaks of 1933 and 1934 show how well this parasite can prosper far from the native haunts of dark skins and palm trees. In many parts of the tropics incidences of 30 to 60 per cent have been reported; in some Egyptian villages near Cairo where careful repeated examinations were made by personnel of the U.S. Naval Medical Unit No. 3 and by the writer, the incidence of what is morphologically *E. histolytica* approaches, if it does not actually reach, 100 per cent in people over one year of age.

Infants under a year old are rarely infected with this or other amebas, although they frequently harbor flagellates. The incidence gradually increases during childhood and usually reaches its highest incidence in young adults. There seems to be no racial discrimination against the organism. In areas where moderate incidences of 5 to 20 per cent occur, there are usually about twice as many *E. coli* infections, probably

because the thicker and more resistant cyst wall of that species makes its transmission easier.

Morphology. The trophozoites of *E. histolytica* (Fig. 12) are large, usually 20 to 30 μ in diameter in the tissue-invading, erythrocyte-eating forms, but smaller, usually 12 to 15 μ in diameter in the lumen-dwelling *minuta* form and in the small-cyst race. The amebas have a thick outer layer of clear, refractile ectoplasm enclosing the more fluid granular endoplasm. In the fresh state, when warm, the amebas are very active, and travel along in a straight line in a manner which Dobell describes as suggesting a slug moving at express speed. In this condition the rapidly advancing end of the body consists of a single clear pseudopodium, while ingested red corpuscles, if present, flow and roll about as though in a mobile liquid. Other amebas have more tendency to stay in one place, where they extend and retract their pseudopodia without making much headway.

After stools have been passed and allowed to cool, the amebas become abnormal and die quickly. The amebas under these circumstances remain in one place and throw out large, dome-shaped, clear pseudopodia from different parts of the body; the endoplasm becomes full of vacuoles, and bacteria invade the dying body. The nucleus also disintegrates and presents abnormal appearances in both fresh and stained preparations. Even in this condition the large amount of clear ectoplasm serves as a means of differentiation from *E. coli*.

The nucleus is so delicate in structure that it is practically invisible in fresh active forms except under a phase contrast microscope. After being fixed and stained the nucleus has a characteristic structure. The nuclear membrane is encrusted with uniform fine granules of chromatin, and a small dot-like central endosome is surrounded by an indefinite, clear halo. Between the endosome and the nuclear membrane is a clear area devoid of granules, marked by a linin network which often has a spoke-like radial arrangement. *E. coli*, on the other hand, has coarser and more irregular peripheral granules and a larger endosome, eccentric in position, with a more definite halo and with a few chromatin granules strung on the linin network surrounding the halo; the nucleus of this species is visible as a bright refractile ring in fresh, living organisms. When stained with iodine the nuclear membrane and endosome of entamoebas show as refractile bodies, and the cytoplasm stains a greenish yellow.

E. histolytica multiplies by simple fission and a modified form of mitosis in which, according to Kofoid and Swezy, six chromosomes are formed. When preparing to encyst, the amebas become smaller and rounded, lose their food vacuoles, and then lay down the delicate cyst

wall. The relatively large nucleus then divides into two and then four progressively smaller ones, but with the same morphology as the nucleus of the trophozoite. Rarely, *E. histolytica* overshoots the mark and produces eight nuclei in a cyst.

Most precystic or young cystic amebas (Fig. 12B and D) lay down in the cytoplasm one or two bar-shaped chromatoid bodies which are refractile in living or iodine-stained cysts and which stain deep black with iron hematoxylin; these chromatoid bodies are quite different from the less massive splinter-like ones found in *E. coli*. In most young cysts there is some stored glycogen, usually in less well-defined vacuoles than in young cysts of *E. coli*. Both the chromatoid bodies and the glycogen vacuoles disappear as the cysts grow older. In fresh preparations the cysts have a faintly greenish tint and are refractile; if a preparation containing numerous cysts is viewed with a low-power objective slightly out of focus the cysts appear as little shining spheres. The size of the cysts varies from about 5 to 20 μ in diameter. As noted on p. 81, there is a small-cyst and a large-cyst race. The former has cysts less than 10 μ (mean 7 to 8 μ) in diameter, the latter has cysts over 10 μ (mean 12 μ) in diameter; the large-cyst race, even when the trophozoites are in the lumen-dwelling *minuta* phase, produce large cysts.

The mature four-nucleated cysts of *E. histolytica* are characteristic enough for any trained technician to be able to identify them. Their differentiation from those of *E. coli* and *Endolimax nana*, with which they are most likely to be confused, is indicated by the table below:

	<i>Entamoeba histolytica</i>	<i>Entamoeba coli</i>	<i>Endolimax nana</i>
Size	5-20 μ	10-33 μ	4 \times 5 μ - 10 \times 14 μ
Shape	Round	Round	Usually oval
Nuclei, number	Usually 4	Usually 8	Usually 4
Nuclear structure	Membrane encrusted with fine chromatin granules; small central endosome	Membrane encrusted with coarser granules; larger, usually eccentric endosome; a few scattered chromatin granules	Chromatin in a single or lobed mass, large relative to size of nucleus
Chromatoid bodies (when present)	Bar-like	Splinter-like	Absent or dot-like
Glycogen vacuoles (when present)	Usually diffuse, ill-defined	May be fairly well defined	None

Habits and Biology. Like most other parasitic amebas, *Entamoeba histolytica* is normally an inhabitant of the large intestine, frequently invading the appendix and occasionally venturing into the lower part of the small intestine. Although amebic ulcers may be found anywhere along the 6 ft. of the large intestine from ileocecal valve to anus, they

are most frequent in the cecum and ascending colon, and next most frequent at the opposite end, in the sigmoid flexure and rectum. These are the regions where the contents of the intestine are usually allowed a temporary halt in their otherwise rough and restless journey through the alimentary canal.

The motile forms, or trophozoites, live for only a few hours after leaving the body even if the feces are kept warm, and they are killed immediately by drying, acids, or other unfavorable conditions.

Cysts have never been found in the tissues except in the liver of dogs fed with raw liver or liver extract. They apparently form in the lumen of the large intestine, and are often passed before they have fully matured, but they are capable of completing their development outside the body if the cyst wall has been formed. The cysts are rarely found in liquid stools, in which the trophozoites frequently abound, but they are often the only forms present in normal formed stools.

The cysts, if kept moist and cool, will live for a number of weeks outside the body. They may remain viable for a week or two in feces if kept cool, and for as long as 10 days in water at room temperature. In a refrigerator they can be kept alive in water for 6 or 7 weeks. They will not stand desiccation, however, and have been found to die in 5 to 10 minutes when dried on the hands. They will live 24 to 48 hours in the intestines of either flies or roaches. Although cold is favorable for their survival (this in itself is enough to throw suspicion on their limitation to the tropics), they are susceptible to moderately high temperatures, even as low as 115° to 120°F. They are therefore killed by pasteurization of milk and by heating of water; heating and filtration are the only practicable methods yet known for destroying them in drinking water. Their specific gravity is only about 1.06, so they settle very slowly in contaminated water; it is estimated that it would take them 4 days to settle 10 feet in perfectly quiet water.

Food Habits, Races, and Tissue Invasion. As already noted, when in the lumen of the intestine in symptomless cases, the amebas commonly do not contain food vacuoles, although ingested bacteria or other debris are sometimes seen, but tissue invaders freely ingest red blood cells. In fact, this is the sole ingested food; the number engulfed usually ranges from one to ten, but may reach forty. *E. coli*, which eats without discrimination, may occasionally ingest a red cell if available, but any ameba found in a dysenteric stool and containing only red cells may safely be regarded as *E. histolytica*. In cultures the amebas "go native" and feed voraciously on bacteria and starch grains. (For culture methods, see p. 85.) Hoare (1952), who recognizes the large-race and small-race forms as distinct species, and considers

the small-race form as harmless as *E. coli*, summarized evidence that even the large-race form has a commensal, lumen-dwelling phase in which it ingests bacteria and in which the trophozoites are very small, whence the name "*minuta* form." However, it seems to the writer probable that these amebas would apply themselves to the surface of the mucous membrane, as they do to solid surfaces in cultures, and then by their lytic excretions dissolve the superficial cells and nourish themselves on the cell juices. The relative infrequency of solid food in the food vacuoles supports this idea.

Under favorable conditions, e.g., low host resistance, and with help in the form of a mucous membrane irritated by chemicals, injured by bacteria, viruses, or worms, or unhealthy due to malnutrition, tissue invasion may occur, ulcers develop, and dysentery or other symptoms follow. The extent to which the amebas are equipped with the enzyme hyaluronidase, which facilitates tissue penetration, may also be a factor, but inconsistent results have been obtained in efforts to demonstrate this enzyme in *E. histolytica*.

Tissue-invading forms, perhaps because of their ingestion of red blood corpuscles and their complete immersion in nutritious cellular food, grow larger in size and cease to produce cysts.

Although some workers have claimed that *E. histolytica* is invariably a tissue invader, James, way back in 1928, called attention to the fact that the numbers of amebas often found in the stools makes it incredible that they all came from invaded tissues. Since amebas in tissues do not form cysts, the tissue invasion that seems to occur only in a minority of cases should not be considered the usual, or even the normal, state of affairs.

Infection in Other Animals. As noted on p. 84, *E. histolytica* can be transferred to many other animals, and natural infections occur commonly in monkeys, occasionally in rats, and probably frequently in pigs. Rabbits, guinea pigs, hamsters, rats, kittens, and dogs are all useful laboratory animals for the study of experimental amebic infections, although they usually have to be infected by special methods such as intracecal injection, by duodenal tube, or through the anus. Hegner in 1932 showed that New World monkeys often show severe amebic lesions when inoculated. Recently it was claimed that Old World monkeys were more like man in being relatively refractory, but these monkeys, in contrast to Hegner's, were previously infected ones, and the influence of immunity was overlooked. In dogs and kittens, the amebas do not produce cysts unless the hosts are fed liver.

Pathogenicity. 1. NON-DYSENTERIC INFECTIONS. Although amebiasis is usually thought of as the cause of dysentery with blood and

mucus stools, or of liver abscesses, these conditions are actually the exception rather than the rule, and some workers have reported that as many as 90 per cent of the dysentery cases in temperate climates are apparently symptomless. Even in the tropics dysentery is exceptional; in an examination by the writer of 500 stools of Egyptian villagers, nearly 100 per cent of which had contained amebas with *E. histolytica* morphology, only four of the stools were suggestive of dysentery. Faust (1941) found *E. histolytica* in 13 (6.5 per cent) of 202 autopsies of persons who had suffered sudden accidental death in New Orleans, but in only 5 of these were amebic lesions demonstrated, and these were superficial, confined to the mucosa. Craig, on the other hand, stated that in his experience 65 per cent of so-called "carriers" have symptoms referable to their infection, which disappear after eradication of the parasite. Sapero (1939), in a study of 216 non-dysenteric cases, found symptoms in 100 of them, in many cases trivial, but often severe enough to require hospitalization.

On the other hand, Miller and Gilani (1951) found that a group of patients in Calcutta who harbored *E. histolytica* and had chronic gastrointestinal symptoms but not dysentery showed no better response to treatment with amebicidal drugs than did a group with similar complaints but no amebas. Obviously, further study is necessary to show just how much non-dysenteric symptoms really are due to amebic infection, otherwise the discovery of amebas in the stool might be misleading and postpone a correct diagnosis. The symptoms commonly associated with chronic amebiasis are abdominal pain, nausea, flatulence, and bowel irregularity, with headaches, fatigability, and nervousness in a minority of cases. The symptoms resemble those of many other gastro-intestinal disorders, particularly appendicitis and peptic ulcer. Appendicitis, or pains simulating it, are frequent enough so that Craig (1944) believed that in all cases of suspected appendicitis an examination for *E. histolytica* should be made, and, if found, amebic treatment should be given before resorting to operation.

2. AMEBIC DYSENTERY. Although the small-race amebas appear to be harmless commensals, at least in the majority of cases, the large race may, under favorable conditions, as noted on p. 81, eat into the tissues, first destroying the mucosa (Fig. 15) and then pushing deeper into the submucosa (Fig. 16), where they spread out and produce flask-shaped ulcers. The abscesses extrude their contents into the intestine as necrosis becomes complete, causing the edges of the injured mucous membrane to cave in, giving a crater-like effect. Sometimes several undermining abscesses coalesce under the surface. Fortunately, the muscular coats of the intestinal wall usually act as a barrier, but some-

times this layer is penetrated by way of the connective tissue sheaths, and the amebas reach the serous membrane, causing extensive adhesions or dangerous perforations. The ulcers vary greatly in number and size; in severe cases almost the entire colon is undermined. When not

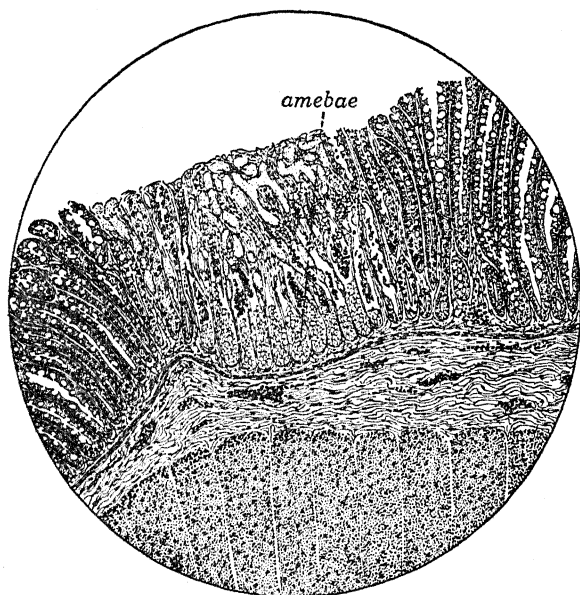


FIG. 15. Section of colon of cat showing an amebic ulcer limited to the mucous membrane. Note broken-down and necrotic epithelium of invaded glands, extravasated blood, and masses of amebae at bottom of glands. (Drawn from slide prepared by H. E. Meleney.)

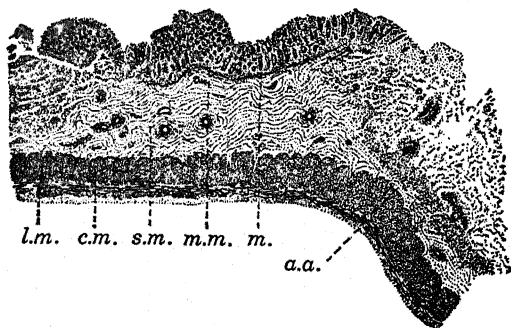


FIG. 16. Section of human colon showing deep amebic ulcer broken through into the submucosa. Note abnormal thickening (edema) of submucosa and pus-like contents of ulcer; *l.m.*, longitudinal muscle layer; *c.m.*, circular muscle layer; *s.m.*, submucosa; *m.m.*, muscularis mucosae; *m.*, mucosa; *a.a.*, amebic abscess. (Drawn from slide prepared by H. E. Meleney.)

invaded by bacteria, the ulcers show no signs of inflammation, but invasion by bacteria often occurs. Sometimes amebic granulomata form in the colon and may be confused with cancerous growths.

The ulceration of the bowel, as noted previously, may produce severe dysentery, though it does so in a minority of cases. The reason for the greater frequency of dysentery in the tropics has been the subject of much speculation, and although, as already noted, some authors have attributed it to the existence in temperate climates of fixed races of very low virulence, others, notably Brug, believe that a tropical climate in itself favors the production of dysenteric symptoms.

In amebic dysentery the stools, usually acid, consist of almost pure blood and mucus, in which swarms of amebas, laden with blood corpuscles, are usually present. The patient is literally "pot-bound," owing to the rectal straining and intense griping pains, with the passage of blood and mucus stools every few minutes. In uncomplicated cases there is little or no fever, a point which is sometimes useful in differentiating amebic from bacillary dysentery. Recurring symptoms sometimes manifest themselves over a period of 30 to 40 years or even longer, and there may be latent periods lasting for at least 6 or 8 years. D'Antoni has suggested that many infections in young adults may have been acquired during early childhood from infected mothers.

3. ABSCESSES IN LIVER, LUNG, ETC. It is clear that invading amebas, actively dissolving the tissues, may frequently be drawn into the portal circulation. Such amebas are carried to the liver and sometimes settle there, attacking the liver tissue. In view, however, of the frequency with which amebas are undoubtedly carried to the liver from intestinal ulcers it is evident that this organ must have a high natural resistance to infection. Nevertheless, small or temporary amebic infections of the liver are probably much commoner than we usually think; sometimes liver abscesses develop without any preceding attack of dysentery. The abscesses are usually sterile so far as bacteria are concerned, although they are sometimes secondarily infected; they may become very large and filled with a slimy, bloody, chocolate-colored material resembling pus, but made up of dead amebas, blood, and fibrous tissue left by the amebas, with active amebas in the enlarging walls. The patient has pain in the liver region, fever, and a high leucocyte count, and his face presents a sorrowful aspect of weariness and apathy, with sallow skin, sunken cheeks, and dark-circled eyes.

Amebas which have escaped into the blood stream are not necessarily halted in the liver but may be carried to any part of the body. Lung abscesses are fairly frequent; these are usually caused by direct extension from a liver abscess through the diaphragm. Such an abscess may

rupture into the pleural or pericardial cavity, but it usually works directly into the lung tissue where the lung adheres to the diseased diaphragm. The lung abscess in turn usually ruptures into a bronchial tube and discharges a brown mucoid material which is coughed out with the sputum. Next in frequency are abscesses of the brain. Abscesses elsewhere are rare. Skin infections, however, may develop about the incisions made for surgical treatment of amebic abscesses.



FIG. 17. Multiple amebic abscesses of the liver. (About $\frac{1}{2}$ diameter.) (From photograph by Sir Philip Manson-Bahr.)

Factors Determining Pathogenicity. There is no doubt that chronic infections with indefinite symptoms are the rule, with the amebas localized in the large intestine or liver. Whether an amebic infection produces acute dysentery, a chronic state of vague discomfort, or no obvious symptoms at all probably depends on several factors, some of which have already been discussed, e.g., races or strains of amebas, and their possible production of hyaluronidase. The importance of irritation of the intestine by chemical means was demonstrated by Nauss and Rappaport, and the importance of bacterial irritation was well shown by Westphal (1948) in a study of intestinal disturbances in German troops in North Africa. He found evidence that amebic infections tended to remain chronic, non-dysenteric, lumen infections until resistance to tissue penetration was lowered by intercurrent bacterial infections. In his experience tissue invasion occurs in about one third of *E. histolytica* carriers who acquire bacillary intestinal infections.

Diet has a great influence. High protein diets are unfavorable for the parasites owing to unfavorable effects on the environment (see p. 119), and adequate protein is necessary to permit the development of immunity (see p. 25). Milk is beneficial in monkey infections, but apparently not in rodent infections. Lack of vitamin C in guinea pigs

(Sadun, Braden, and Faust, 1951), and of niacin in dogs (Larsh, 1952), lowers resistance to amebiasis. Raw liver or liver extract (by mouth but not by injection) benefits dogs with amebiasis just as it does dogs with black-tongue, a disease due to niacin deficiency. Human beings suffering from amebic infections sometimes lose their symptoms promptly when put on a diet rich in proteins and vitamins.

Immunity undoubtedly plays an important part, as Swartzwelder and Avant (1952) showed in the case of dogs and of rats. As in other parasitic infections, antibodies undoubtedly help keep the disease in check, at least so far as tissue invasion is concerned. When the antibodies fall off, there may be relapses from renewed invasion from the lumen of the gut. As mentioned earlier, the immunity may be due in part to reactions against hyaluronidase or other enzymes necessary to invading amebas as well as to the body substance of the amebas.

Mode of Infection and Epidemiology. Since only the cysts can survive outside the body, these alone are concerned in transmission. The trophozoites are rarely capable of passing through the human stomach and intestine to reach their promised land in the colon. Since dysenteric cases rarely pass cysts, they are not usually concerned in transmission; persons who are cyst-passers with few or no symptoms are principally concerned. Even the cysts probably find the stomach a dangerous hazard and, like typhoid organisms, may cause infection more readily when ingested with water than with food because of the greater rapidity with which they pass the stomach. It also throws light on the relative frequency of amebic infections in individuals with abnormally low stomach acidity.

Since amebic cysts survive for considerable periods outside the body if not desiccated (up to 8 days in soil), it is obvious that if they get into drinking water or moist foods, such as raw vegetables, they are in an advantageous position both from the standpoint of length of life and of opportunities to "thumb a ride" into a human alimentary canal. Polluted water is undoubtedly one of the most important means of transmission, and wherever unprotected or untreated ground water is used for drinking in areas where there is widespread soil pollution, amebic infections will be common. Such conditions prevail over vast portions of the tropics and in the rural areas of our own southern states.

Even when a purified water system prevails, accidents may lead to widespread outbreaks of water-borne infections. One hazard is in defective plumbing. The basements of hotels and public buildings frequently contain a veritable maze of pipes, gradually built up, repaired, and replaced throughout a generation or more, and it is not as surprising as it seems at first that errors in plumbing should be made. This

was strikingly demonstrated by an outbreak during the Chicago World's Fair in 1933 in which defective plumbing caused almost 1000 known cases of amebiasis and 58 deaths scattered over 206 cities. The plumbing hazards included back siphonage from sanitary fixtures into water lines, leakage of sewer pipes into basements, and even cross connections between sewer pipes and water pipes made by careless and muddled plumbers. Such faults in plumbing seem to be surprisingly common, but only exceptionally do they cause explosive epidemics. Chlorination of water in most cities prevents sewage-tainted supplies from causing typhoid or other bacterial infections, but it has no effect on protozoan cysts. Sand filtration, properly carried out, seems to remove the cysts very well. It seems probable that amebic infections might be acquired from dirty swimming pools if very much of the water is swallowed.

Although it has been shown that cysts survive for only a few minutes on hands, except under long, closely fitting fingernails, and that the chances are against transmission by soiled hands of food handlers on any single occasion; nevertheless there is no doubt that oft-repeated exposure of one's food to handling by careless, infected food handlers is dangerous. Although cyst-passing cooks, dairy workers, icemen, waitresses, etc., must all occasionally transmit amebic infection, probably housewives and mothers are most important, since the frequency of exposure is greatest. However, the fact that food handlers do not transmit infection as readily as was once supposed is comforting news for those whose gastronomical needs are ministered to by native servants, public food handlers, or rural southern hospitality.

Animal carriers probably do not contribute to human infection, but flies and roaches may do so. Pipkin (1949) showed that filth flies are capable of passing viable cysts in their vomitus up to an hour after ingesting them, and in their feces for over four hours. Flies probably play some part in transmission in unsanitary communities, and may occasionally be an important factor in local outbreaks; Craig described one such outbreak in some troops in El Paso, Texas, in 1916.

Diagnosis. This should usually be based on the finding of *Entamoeba histolytica* in the stools by the methods described on pp. 86-87. Complement fixation and cultural methods were discussed on pp. 85, 87-88. In examining dysenteric stools for trophozoites, special attention should be paid to flakes of blood or mucus. When clinical manifestations of infection are present, a high percentage of cases can be diagnosed by a single examination of a stool or of the rectum by a proctoscope. The presence of whetstone-shaped "Charcot-Leyden" crystals in feces is usually indicative of *E. histolytica* infection.

Experience in identifying Protozoa is required. As great danger lies in making a false positive diagnosis as a false negative one, for to inexperienced workers an ameba is an ameba, and often even epithelial cells and other objects are amebas. Many a patient, unfortunate enough to have an indiscriminating technician mistake leucocytes in a bacillary dysentery stool or find an innocent *E. coli* or *Endolimax nana*, has had to submit to a course of treatment which was useless if not injurious to himself and quite innocuous to the amebas. Dobell in 1917 wrote: "The errors committed by an examiner with little or no previous experience are such as I could not have believed possible if I had not actually encountered them; and in cases where the health of the patient is at stake, it is, I believe, almost better that no examination at all should be made, than that it should be made by an incompetent and inexperienced person."

Treatment. Like many other protozoan diseases, amebiasis if left untreated tends to become chronic and to persist indefinitely. Since the amebas are found both on the surface of the mucosal cells in the lumen and buried in the tissues, permanent cure requires a drug or drugs that will reach them in either situation. Different drugs are needed (1) to stop acute dysentery promptly, (2) to eliminate acute or chronic infections from the intestine, and (3) to cure hepatic, pulmonary, or other extra-intestinal infections.

For prompt relief of acute or subacute dysentery, emetin was long the drug of choice in spite of its toxicity and the fact that it has to be given by injection, but certain antibiotics—Fumagillin, Terramycin, Erythromycin, and Aureomycin—are more effective, and can be given by mouth. Also said to be effective is conessine, an extract of kurchi, which is also less toxic than emetin, and given by mouth.

For eradication of intestinal infections after the dysentery is controlled, or in chronic cases, certain arsenic compounds (Carbarsone, Thiocarbarsone, Milibis) and a number of iodine compounds (Chinifon (Yatren), Diodoquin, and Vioform) are effective when given over a period of 7 to 10 days (for doses of Carbarsone and iodine compounds see Craig, 1944 or Faust, 1954). Milibis is a very insoluble compound; 0.5 grams can be given to adults three times daily after meals for 7 days. Half this amount can be given to children. Except where there is acute dysentery the arsenic and iodine compounds are still the drugs of choice even though the antibiotics may also be effective, because the latter sometimes cause serious disturbances, with elimination of the normal bacterial flora of the intestine. Like many other upsets of the balance of nature, this may have very undesirable effects.

For amebiasis of the liver or lungs, or other extra-intestinal amebic

infections, emetin, long the only effective drug known, has been almost entirely superseded by the anti-malarial drug, Chloroquine. The results are dramatic; apparent cures occur in a week, though treatment should be continued with reduced dosage for 2 or 3 weeks. Conan (1948) got good results with 0.3 gram of the base twice daily for 2 days, followed by sustaining doses of 0.3 gram daily for 12 to 19 days more. One recommended regimen is one 0.25 gram tablet of Chloroquine diphosphate every 6 hours for 4 days, then 1 twice daily for 7 days, and then 1 daily to the twenty-first day, given after food.

Because intestinal infections may be cured without affecting incipient liver infections, Berberian et al. (1952) tried treatment and subsequent prophylaxis with a combination of Milibis and Chloroquine, and found it very successful. Martin et al. (1953) experimented with a number of drugs singly and in combination in a group of 538 acute infections in Korea. They found that Terramycin alone or in combination with emetin, Carbarsone, Chiniofon, or Chloroquine; Milibis and Chloroquine; and Aureomycin and Chloroquine all gave excellent initial responses and low relapse rates. They did not use Fumagillin, which could probably be substituted for either of the other antibiotics.

Diodoquin, a non-toxic drug, was recommended by Craig as a prophylactic for travelers in places where there is danger of infection. A new non-metallic organic compound, Camoform, shows promise of being useful for both intestinal and extra-intestinal amebiasis.

Prevention. The essentials in the prevention of amebic infection are sanitation and protection of water and vegetables from pollution. Soil pollution, especially by use of night soil, is dangerous in places where unfiltered water is used for drinking, even if it is chlorinated. Clark showed that there was a great falling off of amebic dysentery in Panama after a good water system was installed in 1914-1915. In view of the plumbing hazards discovered in Chicago in 1933 it seems evident that public health officials and city governments should spend sufficient money for inspection of hotels and public buildings, but for the most part they have not done so.

Vegetables such as lettuce, radishes, and strawberries, grown in ground fertilized by night soil or even in ground subject to ordinary pollution, are dangerous. Beaver and Deschamps (1949) recommend immersion in 5 per cent acetic acid (or vinegar) for 15 minutes at 30°C. or in 2.5 per cent for 5 minutes at 45°C. It is customary for Europeans in India to soak uncooked vegetables in a potassium permanganate solution for an hour, but usually several cooks have to be discharged before one is found who will actually carry out what he considers a silly notion rather than risk being caught not doing it. Even then he

feels that if he sets a head of lettuce in an inch of "red water" he has sufficiently carried out instructions. Immersion for 30 seconds in water at about 150°F. has also been recommended.

Although transmission by the hands may not be so easy as was once supposed, Craig believes that food handlers constitute the most important means of transmission in sanitated cities. The tendency for the infection to spread in families indicates transmission from person to person, probably as a rule from the servant or housewife who prepares the food. Continually repeated exposure may be dangerous when occasional exposure is not. A careful washing of the hands with soap and water after using a toilet would probably eliminate most of the danger. James recommended that Europeans in the tropics should insist on all servants cleaning their hands thoroughly with scrubbing brush, antiseptic soap, and water several times a day, especially before preparing or serving food. This is excellent advice, but in India, at least, one would have to stand over each servant with both eyes wide open during the entire process of each washing and would very likely have to render assistance!

Other Intestinal Amebas

The other amebas which inhabit the human intestine, with the exception of *Dientamoeba fragilis*, would be of very little consequence if it were not for the danger of confusion between them and *Entamoeba histolytica*. They are never tissue parasites, and there is no good evidence that a human being is any worse off for harboring these guests in his intestine. They ordinarily live free in the lumen of the intestine, where they feed on bacteria, small cysts, starch grains, and all sorts of debris found in the semifluid medium in which they live. In other respects, such as life cycle, cultural characteristics, mode of transmission, transferability to other kinds of animals, etc., they appear to be similar to *E. histolytica*.

***Entamoeba coli*.** This is the commonest species of ameba in the human intestine and has been stated to occur probably in 50 per cent of human beings; its distribution is world-wide. According to Dobell "no race, nor any country, has yet been discovered in which infections with this species are not common." In the United States it has roughly about 3 times the incidence of *E. histolytica*. The motile forms are found especially in the upper part of the large intestine, and the pre-cystic and cyst forms lower down.

The outstanding characteristics of *E. coli* (Fig. 13) have been mentioned in connection with its differentiation from *E. histolytica*, but they may advantageously be summarized again. The living forms are

usually 20 to 30 μ in diameter and are never as small as the smallest races of *histolytica*. The body usually has very little ectoplasm, and even the ponderous pseudopodia are usually composed mainly of endoplasm, although clear ones are occasionally produced. Unlike *histolytica* this ameba tends to move about sluggishly in one place without making much headway in any one direction. The body is usually crammed with food vacuoles, for it is a voracious and indiscriminating feeder. The nucleus is visible in living specimens as a refractile ring.

In stained specimens the contained food and the nucleus distinguish it from *histolytica*. The nucleus has a coarser peripheral layer of chromatin, a larger and eccentrically placed endosome, and usually dots of chromatin strung on the linin network.

The precyst stages are the most difficult to distinguish from those of *histolytica*; the distinction can be made only by observation of the nuclear structure in good specimens; the 2-nucleated stage (Fig. 13B) usually has a very large glycogen vacuole, which nearly fills the cyst, lying between the nuclei, but this begins to become diffuse even by the time the cyst becomes 4-nucleated. The mature cysts, which are most commonly found in fresh stools, are 15 to 22 μ in diameter, have 8 nuclei of the typical *coli* type, more granular cytoplasm than in *histolytica*, and either no chromatoid bodies or else a few flakes like splintered glass, but never the heavy bars found in young *histolytica* cysts. According to Hegner, the cysts hatch as entire 8-nucleated amebas.

***Endolimax nana*.** This little ameba is almost as frequent an inhabitant of the human intestine as is *Entamoeba coli*, and is frequently found in 15 to 30 per cent of cases in routine examinations in this country. Its principal characteristics are those given under the genus *Endolimax* on p. 82 and shown in Fig. 14A and A'. It is a very small ameba, varying from 6 to 12 or 15 μ in diameter, but usually averaging only about 7 to 9 μ . It creeps sluggishly like *E. coli* and often contains numerous food vacuoles filled with bacteria. The 4-nucleated cysts (Fig. 14A') are distinguishable by their small size (usually 6 to 10 μ by 5 to 8 μ), their usually oval shape, and the peculiar structure of the nuclei, described on p. 82. Like *E. coli*, it cannot be eliminated by drugs although it temporarily disappears during emetin treatment. *Endolimax nana* also occurs in monkeys, and probably identical forms occur in rats and pigs; a form from a guinea pig differing only in its smaller size has also been described. Other probably different species occur in frogs, lizards, and fowls.

***Iodamoeba bütschlii*.** This small ameba is usually larger than *Endolimax nana* and smaller than the entamebas. Usually the amebas

average about 9 to 11 μ in diameter, but specimens varying from 4 to 19 μ have been found, and Wenrich (1937) believes that there are large and small races. The characteristic features of the nucleus are mentioned on p. 82, and shown in Fig. 14B and B'. The living trophozoites are sluggish but move about by the extrusion of clear ectoplasmic pseudopodia; the nucleus is not usually visible, but there are usually ingested food particles. In stained specimens the body does not usually show any clear ectoplasm and often has a vacuolated appearance.

The cysts of this ameba are peculiar in several respects. They are about the same size as the trophozoites and are of irregular shape, as if formed under pressure. The endosome moves to an eccentric position almost in contact with the nuclear membrane, and the granules between it and the periphery usually cluster into a crescent-shaped mass on the inner side of it. Usually the nucleus remains single, but Wenrich states that occasionally cysts with two or even three nuclei are formed. The most striking feature of the cysts, however, is a large, sharply defined vacuole filled with glycogen and therefore staining brown in iodine. In fixed and stained specimens the glycogen dissolves out and leaves a large cavity.

Iodamoeba bütschlii infests a very high percentage of monkeys and pigs. Cauchemez estimated that 50 per cent or more pigs in France are infected, and Feibel found 20 per cent of pigs slaughtered in Hamburg harboring it. The pig may, in fact, be considered the normal host in temperate climates. This is another example of the close parasitological relations between pigs and man. This ameba is not so common in man as those hitherto described; in most surveys in this country it occurs in 2 to 6 percent, especially of adults. Much higher incidences have been reported in Mexico and China, and in some Egyptian villages the incidence is over 50 per cent, in spite of the fact that pigs are absolutely taboo.

There is one unique and amazing instance of fatal generalized amebiasis in a Japanese soldier, captured in New Guinea. There were amebic ulcers in his digestive tract from stomach to colon, and also in his lymph nodes, lungs, and brain (but not in his liver), in which the amebas were definitely not *Entamoeba histolytica*, but either *Iodamoeba bütschlii* or one closely resembling it (Derrick, 1948).

Dientamoeba fragilis. This is another small ameba, usually ranging in size from 3.5 to 12 μ ; the average is usually around 9 μ , but in diarrheic stools it may be 11 μ . This ameba (Fig. 14C and C') is peculiar in that, in most populations of it, about 80 per cent have two nuclei, and occasionally supernucleate forms appear. This is due to the fact that, unlike other amebas, the nucleus divides shortly after cell division

instead of just before it. The nucleus has in its center a cluster of four to eight deep-staining granules, one of which is an endosome. The cytoplasm has a granular or frothy appearance, with or without food vacuoles, and often the ectoplasm is sharply demarcated from the endoplasm by a deep-staining zone. This and other characters of the nucleus and cytoplasm have led both Dobell and Wenrich to suggest relationships to the flagellate *Histomonas* (Fig. 24); Dobell says that "*Dientamoeba* is, indeed, a typical flagellate except for the important circumstance that it possesses no flagella." No cysts are formed by *Dientamoeba*. In living or iodine-stained specimens the nuclei are not visible, and they stain poorly in MIF. In saline suspensions the trophozoites remain in a sort of dazed, immobile state for 5 or 10 minutes, appearing rounded and granular; they then extrude broad, flat, leaf-like pseudopodia of clear ectoplasm. In tap water they swell up and explode, leaving a hollow shell of ectoplasm.

Dientamoeba has a world-wide distribution, and its incidence is probably much higher than commonly reported, partly because methods suitable for its detection are not used and partly because many technicians fail to recognize it when they see it. Wenrich and his co-workers found it in 4.3 per cent of 1060 students at the University of Pennsylvania and in 3.9 per cent of 190 Philadelphia food handlers, when only a single stool was examined; with more examinations an incidence of 7.4 per cent was obtained in the latter group. In some institutions incidences of 36, 42, and 50 per cent have been obtained. In some Egyptian villages the writer found it in 11 per cent of the population by a single 10-minute stool examination in MIF. Yet Wenrich (1944) reported that, in 19 surveys in the United States between 1934 and 1944, 65,253 persons were examined without this elusive organism being found in any of them! The organism is best recognized in smears fixed with picro-formol-acetic in the proportions of 75:15:10, and stained with iron hematoxylin. In the group of 1060 students mentioned above, over 60 per cent of the *Dientamoeba* infections were recognized only on stained slides.

There is strong evidence that *Dientamoeba* may sometimes be pathogenic, so, unlike the other amebas except *Entamoeba histolytica*, it is of interest to the medical practitioner as well as to the parasitologist in an ivory tower. Wenrich et al. in 1936 reported a higher incidence of gastro-intestinal disturbances among students playing host to this ameba than among those harboring *Entamoeba histolytica*, and Saper (1939) recorded that 27 per cent of *Dientamoeba* cases had complaints as compared with 43 per cent of those with *E. histolytica*, and 7 per cent of

those devoid of intestinal protozoa or harboring only *Entamoeba coli*, *Endolimax*, or *Iodamoeba*. Wenrich calls attention to frequent eosinophilia in *Dientamoeba* cases. The commonest symptoms associated with it are diarrhea, colicky pains, fatigue, and weight loss. Burrows et al. (1954) found this ameba in 4 of 581 appendices; in every case they were ingesting red corpuscles (though not invading tissues), and they appeared to be the cause of a fibrosis of the walls.

How *Dientamoeba* is transmitted is still an unsolved problem, since the organism usually dies in from a few hours to a day or two in feces, and explodes in water. Dobell failed to infect either himself or two monkeys by means of swallowed cultures, although the infection does occur in monkeys. Dobell's belief that *Dientamoeba* is related to *Histomonas* suggests the possibility that it may be transmitted by the eggs of parasitic worms, since *Histomonas* is transmitted in this manner (see pp. 127-128).

Dientamoeba infections usually respond to Carbarsone and other drugs effective against *E. histolytica*. This in itself is suggestive of its being a pathogenic parasite, for the species of amebas that are content to live a saprophytic life in the lumen of the intestine are unaffected by these drugs.

Mouth Amebas (*Entamoeba gingivalis*)

In contrast to all other amebas living in man or animals, there is one species of *Entamoeba*, *E. gingivalis*, which inhabits the mouth instead of the large intestine. The same or a similar species has been found in pyorrheal pus from the mouths of dogs and cats, around the teeth of horses, and in a high percentage of captive monkeys. Dogs with inflamed gums or pus pockets can be infected with the human mouth ameba. In man it can be found in a high percentage of individuals, increasing with advancing age until, according to Kofoid, 75 per cent or more of people over 40 harbor it.

E. gingivalis markedly resembles *E. histolytica*. It is about 12 to 20 μ in diameter and has crystal-clear ectoplasm (Fig. 18). The vacuolated endoplasm is usually crowded with food particles which seem to float in the center of large, fluid cavities. The pseudopodia are normally broad and rounded, like large blisters, and the ameba normally progresses rapidly in various directions. The nucleus has the peripheral chromatin in rather uneven granules, and the endosome consists of several closely associated granules. Whereas the *E. histolytica* nucleus has a clear halo around the endosome and a finely granular outer zone between the halo and the nuclear membrane, *E.*

gingivalis has a granular, cloudy halo, especially dense around the endosome, and a clear outer zone, through which a few spoke-like strands of linin run.

Unlike its close relatives this species fails to form cysts; apparently the ease and rapidity with which infections can spread from one human mouth to another do away with the biological necessity for cysts. As would be expected of an organism inhabiting the mouth, it is rather more adaptive than the intestinal amebas to changing environmental conditions, e.g., heat and cold, hydrogen-ion concentration, and chemical constituents of a culture medium.

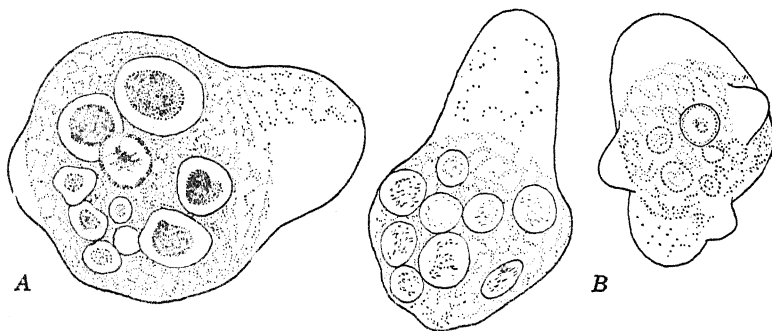


FIG. 18. *Entamoeba gingivalis*: A, stained specimen; B, living specimens; nucleus near center of stained specimen, and visible in unstained specimen at right. (Adapted from Kofoed and Swezy, *Univ. Calif. Publ. Zool.*)

The food vacuoles of *Entamoeba gingivalis* sometimes contain bacteria, but they most often contain the nuclei of leucocytes in various stages of digestion (Fig. 18). Goodey and Wellings in 1917 concluded that these were "salivary corpuscles," i.e., nuclei of disintegrating leucocytes, which are abundant in saliva. In 1926, however, Child found undoubted evidence of the ingestion of whole leucocytes as well as remnants of dead ones, and in cultures Miss Howitt in 1926 found that they ingest both red blood corpuscles and leucocytes. She also observed that red corpuscles lying near them faded from view in a few minutes, indicating cytolytic action, which may also be effective against leucocytes and tissue cells.

Pathogenicity. Although the presence of amebas in the mouth has been known for many years, no one took much interest in them until Bass and Johns in 1914 and Barrett in 1915 demonstrated an apparent relation between these mouth inhabitants and the presence of pus pockets between the teeth and gums, a disease known as pyorrhea, from which a high percentage of human beings suffer. These little pockets erode the delicate periodontal membrane surrounding the roots of the

teeth. Whether the formation of pus pockets is initiated by the amebas is doubtful, but *E. gingivalis* is nearly always, perhaps always, present in the lesions, and at the very bottom of them, often buried in the inflamed tissues.

After this ameba had had the spotlight turned on it for two or three years it fell into obscurity again, because of doubt of its causal relation to pyorrhea, but interest in it was again revived by Kofoed and some of his students. Hinshaw (1926) concluded that protozoan parasites do not occur in normal mouths, whereas *E. gingivalis* occurs in most, if not all, cases of incipient to advanced pyorrhea. Since this ameba ingests both red corpuscles and leucocytes, and can dissolve tissues, the burden of proof falls on those who believe in its innocence. The amebas often cluster about on the strands of filamentous bacteria which are involved in the formation of tartar, and prey upon the nuclei of the swarming leucocytes, without invading the adjacent gum tissue. The bony tissue between the teeth and below the level of the tartar is extensively eroded without accompanying evidence of infection by either bacteria or amebas. The host reacts to the stimulus of this combination of bacteria, amebas, and tartar by an active and continuous accumulation of leucocytes and resulting flow of pus. Even if the amebas do not actually initiate the ulcerations but merely find a pleasant field of activity in them after bacteria have started them, one must be very generous to absolve them from complicity in their extension. The amebas exhibit a peculiar adhesive quality and frequently drag along behind them large clumps of bacteria; such transportation of bacteria to the depths of the pus pockets may in itself be injurious, even if the amebas do not directly attack other tissues than the leucocytes.

E. gingivalis is a common invader of the crypts of infected tonsils, where, as in the mouth, it may be presumed to do some mechanical injury if it does not actually attack the living tissues. It has been found on a few occasions to multiply abundantly in bronchial mucus and appear in sputum, and this could easily lead to a false diagnosis of pulmonary *E. histolytica* infection.

Treatment and Prevention. Ordinary cleanliness of the mouth by frequent brushing of teeth, rinsing of the mouth and care of imperfect teeth is the most important factor in protecting the gums against the formation of pus pockets, but such methods are of little or no avail after the disease has started. No good remedy is known for amebic infections of the mouth.

Though it is still uncertain to what extent, if at all, amebas are involved in causing or aggravating pyorrhea, it would seem to be the course of wisdom to avoid them as far as possible. They are undoubt-

edly spread not only directly from mouth to mouth, as in kissing, but also by minute droplets expelled in coughing or sneezing, and by means of drinking glasses, spoons, etc., on which it is evident that they can live as long as a trace of moisture remains. It is probably impossible, however, to avoid occasional infection with *E. gingivalis*. One cannot always make a protozoological examination of a mouth before indulging in a kiss, nor can one be sure that a cook has not coughed during the preparation of a meal. If, however, the mouth is kept scrupulously clean and in as near perfect condition as possible, the amebas will be less likely to find a congenial place to settle down; in most mouths, on the other hand, plenty of hospitality is offered to them.

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Intestinal Flagellates and Ciliates

Flagellates in General

The flagellates (subphylum Mastigophora) surpass all other Protozoa in numbers of individuals and in variety of environments successfully occupied. Free-living forms range from the "red snows" of Alpine summits to the ooze of the ocean's depths, and they abound in natural waters, soil, decaying organic matter, and, either as commensals or parasites, in the bodies of the majority of species of animals and many plants, where few tissues or organs are immune to their invasions. In their varied forms of nutrition and metabolism they afford valuable material for the study of fundamental biological problems.

Classification. As noted on p. 41, the Mastigophora are divided into two classes, the Phytomastigophorea and the Zoomastigophorea, containing the green alga-like forms (and their allies) and the animal-like forms, respectively. All the flagellates that are parasitic in higher animals belong to the Zoomastigophorea, and there are representatives in four of the five orders. The fifth one, Hypermastigida, contains cellulose-digesting symbionts of termites and roaches, enabling these insects to utilize such things as telegraph poles and old books as food.

Although there is no general agreement on divisions into families, the following arrangement, following Jahn and Jahn, and Hall, is as logical as any:

Class Zoomastigophorea.

Order 1. **Rhizomastigida.** Body ameboid, with pseudopodia, and 1 to 4 flagella. Includes *Histomonas* (see p. 127).

Order 2. **Protomastigida.** One or two flagella; body plastic but not ameboid; no axostyle. Several families, including the following:

Family **Trypanosomidae.** One flagellum ending in a blepharoplast, with a kinetoplast (see p. 35) near it (rarely absent). Includes the hemoflagellates of vertebrates.

Family **Cryptobiidae.** Two flagella, one trailing and adherent to body; large kinetoplast. Parasites of mollusks and digestive tract of fishes. *Cryptobia* and, in blood of fishes, *Trypanoplasma*.

Family **Bodonidae**. Two flagella, one usually trailing in swimming. Some in digestive tract of amphibians and reptiles; mostly saprozoic. *Bodo* and *Cercomonas* often found in stale feces or urine, and sometimes in urinary bladder.

Order 3. **Polymastigida**. A heterogeneous group of flagellates with 3 to 8 flagella (2 in *Retortamonas*) and 1 to several nuclei. No costa (see p. 114), parabasal body, or axostyles, except in Hexamitidae; some free-living, some parasitic; includes 8 families, including the following:

Family **Tetramitidae**. Flagella 3 or 4, with 1 or 2 trailing; 1 nucleus; no cytostome. Includes *Enteromonas* and *Tricercomonas* (if a distinct genus [see p. 126]).

Family **Retortamonadidae**. Flagella 2 or 4, 1 trailing, 1 nucleus; cytostome present with supporting fibrils. Includes *Retortamonas* and *Chilomastix*.

Family **Hexamitidae**. Flagella 6 or 8; 2 nuclei; parabasal bodies and axostyles in some. Includes *Giardia* and *Hexamita*.

Order 4. **Trichomonadida**. Axostyle and costa present. Flagella in one or more groups (mastigonts) of 3 to 6 each, 1 trailing; each mastigont associated with 1 nucleus. In insects, especially termites, and vertebrates.

Family **Trichomonadidae**. Have axostyle, costa, and undulating membrane connecting trailing flagellum to body; 3 to 5 anterior flagella; 1 nucleus. Includes *Trichomonas*.

Order 5. **Hypermastigida**. Numerous flagella and multiple axostyles and parabasal bodies, but 1 nucleus. Parasites of termites and roaches.

For convenience we can divide all the flagellates found in man and domestic animals into two groups, the hemoflagellates and the intestinal flagellates. The hemoflagellates live in the blood, lymph, and tissues of their vertebrate hosts and usually pass one phase of their life cycle in the gut of insects. All these belong to the family Trypanosomidae and will be considered in the next chapter. The intestinal flagellates will be considered in the present chapter, along with the allied forms found in the mouth and vagina. At the end of the chapter we shall also present a brief discussion of intestinal ciliates, only one species of which is a true parasite of man, though many are commensals in the alimentary canals of large herbivorous animals. The coccidians, some of which are important parasites of the digestive tracts of many birds and mammals, will be reserved for consideration in Chapter 10, along with other Sporozoa.

INTESTINAL FLAGELLATES

The human "intestinal" flagellates which are commonly recognized belong to five genera, of which *Trichomonas* lives in the mouth, large intestine, and vagina; *Chilomastix*, and probably the rarer *Retortamonas* and *Enteromonas*, lives in the large intestine; and *Giardia* lives in the small intestine. In addition to these genera we shall briefly consider

Histomonas, a parasite of the intestine, ceca, and liver of turkeys, and *Hexamita*, in the intestine of various birds. Most of these intestinal flagellates form cysts, but neither *Histomonas* nor any of the trichomonads do so. None of these flagellates requires an intermediate host except *Histomonas*, which makes use of the eggs of an intestinal worm (*Heterakis*) for this purpose.

All the intestinal flagellates except *Giardia* are easily cultivated in artificial media and are less fastidious about their culture media than are the amebas, although any medium satisfactory for amebas will also grow the intestinal flagellates. Unlike the amebas, however, the flagellates do not require accompanying bacteria. A simple and successful culture consists of a long slant of 1.5 per cent nutrient agar, without a butt, half covered with a sterile Ringer solution with one-twentieth part of horse serum added. For *Trichomonas vaginalis* the slant should be three-quarters covered, the pH lowered to 5.5 to 6, and 0.2 per cent dextrose added. It has been customary to subculture every few days, but Wenrich found that, if the nutrients and evaporated water are replaced as needed, cultures will live possibly for years.

Some of the intestinal flagellates appear to be harmless commensals; such are *Chilomastix*, *Retortamonas*, and *Enteromonas*. *Trichomonas* and *Giardia*, on the other hand, unquestionably have pathogenic propensities, although some authors tend either to minimize or exaggerate them.

There is still much doubt as to the extent to which intestinal protozoans are confined to particular hosts. Some workers believe that each animal has its own species peculiar to it, and that these species do not normally infect other hosts. Although evidence is accumulating to show that many intestinal protozoans of man are able to live in such animals as monkeys, rats, and hogs, *Giardia* seems to be an exception (see p. 122).

Naturally these parasites are seldom discovered except when there is some intestinal ailment, since in normal health feces are seldom submitted for examination. Where routine examinations have been made regardless of physical condition, it has been found that a large percentage of people in unsanitary places are infected. In examinations of children under a year of age in Egypt (unpublished data by Lawless), flagellates, particularly *Trichomonas* and *Giardia*, are common, whereas amebas usually do not appear until near the end of the children's first year.

It is important to remember that free-living, coprozoic flagellates not infrequently appear in stale specimens of feces or urine, and may be a cause of confusion to unsuspecting technicians. Especially common

are species of *Bodo* and *Cercomonas*, 5 to 10 μ long, both of which have two flagella, one anterior and one trailing. *Bodo* has an indistinct cytostome and a parabasal body, which *Cercomonas* lacks.

Trichomonas

General Morphology. The trichomonads (Fig. 19) are all spindle- or pear-shaped organisms easily recognizable by their free anterior flagella, which are three to five in number, and their undulating membrane. The latter has a flagellum and an accessory fibril along its

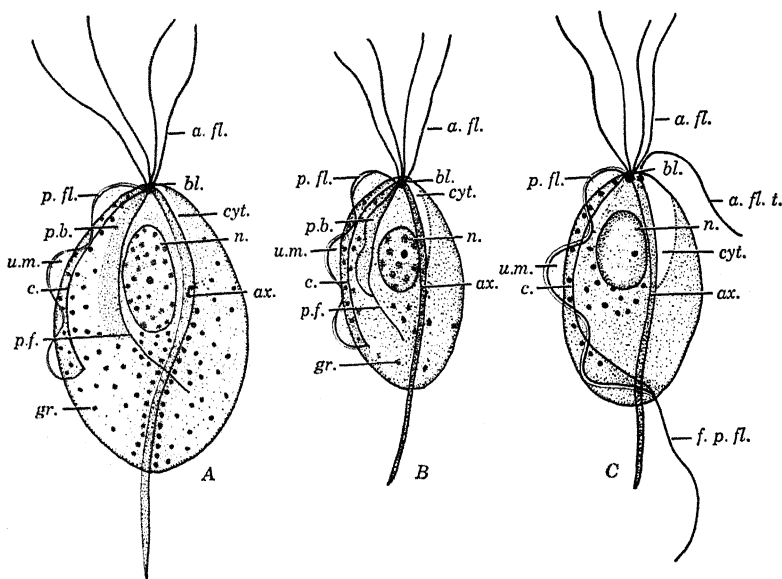


FIG. 19. Trichomonads of man: A, *T. vaginalis*; B, *T. tenax*; C, *T. hominis*. Abbreviations: a.fl., anterior flagella; a.fl.t., anterior trailing flagellum; ax., axostyle; bl., blepharoplast; c., costa; cyt., cytostome; f.p.fl., free posterior flagellum; gr., metachromatic granules; n., nucleus; p.b., parabasal body; p.f., parabasal fibril; p.fl., posterior flagellum with accessory fibril; u.m., undulating membrane. (After Wenrich, *Am. J. Trop. Med.*, 1944.)

outer margin, giving it a double appearance, and a deep-staining basal rod or costa along its attachment to the body. The body is supported by a stiff axostyle often protruding posteriorly like a tail spine. The anterior nucleus is round or oval with varying amounts of chromatin. In most species there is a sausage-shaped parabasal body anteriorly, close to the nucleus, with a posteriorly directed parabasal fiber. In *T. hominis* the parabasal seemed to be lacking, but Kirby (1945) noted a small rounded one in a slightly different position. The anterior

flagella, when three or four in number, arise together from an anterior blepharoplast; when a fifth is present it arises separately and is posteriorly directed. A cytostome is present, in some species well developed, in others vestigial; in the latter there are few or no food vacuoles. All these structures are shown in Figs. 19 and 20.

Species. Many vertebrates, including fish, frogs, reptiles, birds, and mammals, harbor species of *Trichomonas*. Some of these species habitually have three, some four, and some five anterior flagella. By some authors these have been placed in separate genera, *Tritrichomonas*, *Trichomonas*, and *Pentatrichomonas*, respectively. There has long been a belief that the human intestinal species, *T. hominis*, unlike other forms, many have either three, four, or five flagella, but there is still some uncertainty about it, since two or more of the clustered anterior flagella tend to adhere to each other. Kirby (1945) thought the five-flagellated form is the common if not the only form, but Wenrich (1947) hesitated to accept this view. The common five-flagellated form differs from other species not only in having the additional independent flagellum, but also in having a full-length undulating membrane and costa, free posterior flagellum, and a different type of parabasal body. These characteristics seem sufficient to warrant separating these five-flagellated intestinal forms into a separate genus *Pentatrichomonas*. They occur not only in man but also in monkeys, cats, dogs, and rats. Wenrich, however, prefers to be conservative and retain the name *Trichomonas hominis* for the intestinal group until the status of four- and five-flagellated forms is determined.

Many forms of *Trichomonas* show distinctive morphological and physiological characters which warrant their recognition as distinct species. There is, however, no justification for recognizing new species simply because they are found in new hosts, since, to the annoyance of those who adhere to a belief in fairly close host specificity for intestinal Protozoa, many trichomonads are remarkably promiscuous about their hosts. *T. gallinae*, for instance, a common pathogen of pigeons, can establish itself in chickens, turkeys, hawks, parakeets, and sparrows, and *T. hominis* can be established in monkeys, cats, and rats.

Trichomonads are more finicky about their habitats in the body than they are about their hosts. *T. hominis* and *T. gallinarum* inhabit the lower alimentary canal; *T. gallinae* the throat, esophagus, and crop; *T. tenax*, *canistomae*, and *equibuccalis* the gums about the roots of the teeth; *T. vaginalis* the vagina and prostate; and *T. foetus* the vagina and uterus of cows and the preputial cavity of bulls. One three-flagellated species, *T. faecalis*, recovered repeatedly from the feces of a single human being, grew in fecal and hay infusions and was success-

fully established in frogs and tadpoles. Wenrich suspects that this species may be identical with *T. batrachorum* of Amphibia.

Trichomonads vary in pathogenicity from the harmless coprozoic form *T. faecalis* to highly pathogenic species like *T. foetus* and *T. gallinae* (see pp. 119–120). Fortunately the pathogenicity of the species found in man is relatively low.

There has been much dispute as to whether the three species in man—*vaginalis*, *hominis*, and *tenax*—are distinct species, but it is now definitely established that they are, since they differ in both morphology and physiology, and are not transferable from one habitat to another. *T. vaginalis* and *T. tenax* resemble each other more than they resemble *T. hominis*.

Miss Bonestell in 1936 succeeded, as have others, in establishing *T. hominis*, but not *vaginalis* or *tenax*, in the large intestines of kittens, and she could establish *tenax*, but not the others, in the mouths of kittens. *T. vaginalis* has not been established elsewhere than in the human vagina, probably because here alone it finds suitably high acidity (pH 4 to 5).

Biology. Trichomonads swim with a characteristic wobbly or rolling motion; sometimes they use their flagella to whirl their bodies about while anchored to a bit of debris by the axostyle. In worming their way through devious passages they can squeeze their bodies, especially the fore part, into distorted shapes. The intestinal forms feed extensively on bacteria and debris, but the vaginal and buccal forms taken from their natural environment seldom contain any solid food except leucocytes or their remains, although in cultures they contain bacteria. All species feed in part by absorption of dissolved substances, since they can be grown in liquid media containing serum without accompanying bacteria. Johnson, Trussel, and Jahn (1945) were the first to succeed in obtaining bacteria-free cultures of *T. vaginalis*, which they did with the help of penicillin.

Multiplication is by simple fission, but when it is rapid the division of the cytoplasm may fail to keep pace with growth and nuclear division, so that large multinucleate bodies are occasionally formed. No sexual phenomena have been observed.

No evidence exists that any of the species encyst. The trophozoites are apparently hardy enough to live outside the body long enough to be transferred to new hosts. *T. hominis* lives in undiminished numbers for several hours, and in some individuals for days, in the feces, and will survive a day or two in water or milk. *T. tenax* will live for several days in tap water at room temperature; in mixed material Stabler et al. found *T. tenax*, but not *T. vaginalis*, to survive when held at 16°

to 18°C. for 48 hours before incubating at 37°C. *T. vaginalis* survives less readily than the others, and its means of transfer from host to host is somewhat of a mystery, although it is often transmitted venereally, and for brief periods by contaminated toilet seats, etc.

Trichomonas vaginalis (Fig. 19A). This is a very common human parasite. Various authors in many parts of the world have reported it in 20 to 40 per cent or more of women where unselected series of examinations have been made, whereas in series of cases with leucorrhoeic conditions the organism is commonly found in 50 to as many as 70 per cent of the patients examined. The incidence is nearly twice as high in Negro women as in white. It also occurs in 4 to 15 per cent of men.

This is the largest of the trichomonads found in man; it varies in length from about 10 to 30 μ , but most individuals are usually between 15 and 20 μ long. There are four anterior flagella and a short undulating membrane which seldom reaches beyond the middle of the body. The axostyle projects as a slender spike at the posterior end, and the organism is frequently seen to anchor itself to debris by this structure. The nucleus is oval and contains rather scanty chromatin scattered in granules. Deep-staining granules are also abundant in the cytoplasm, many of them in rows beside the axostyle or along the costa. The cytostome is very inconspicuous, and the body contains few food vacuoles. The parabasal apparatus is a sausage-shaped, rather faintly staining body lying beside the nucleus, and a more slender but deeper-staining fibril reaching to near the middle of the body.

T. vaginalis inhabits the vagina primarily, but also invades Skene's glands in the urethra; it is only occasionally found in other parts of the female urinogenital system. In males it occurs in the urethra and prostate. Repeated reinfection from the sexual partner has frequently been found to account for infections in women that seemed refractory to treatment. *T. vaginalis* often grows in abundance in the upper part of the vagina around the cervix but seems to show no tendency to invade the uterus as does *T. foetus* in cattle (see p. 119). It occasionally occurs in the urinary bladder, but care must be taken not to confuse it with coprozoic flagellates (see p. 113), which are frequently found in carelessly collected or stale urine.

The presence of *T. vaginalis* in the vagina is associated with a characteristic acid, creamy-white, frothy discharge which may be very abundant, and which to the experienced eye is usually sufficient for a diagnosis of the infection. The discharge often persists for months or years. The vulva becomes red and chafed, and the mucosa of the vagina and cervix is congested, with a deep red mottling. Some patients

complain of severe itching or irritation in the genital region, but many seem to have no symptoms other than the discharge. That *Trichomonas* is actually the cause of these symptoms has been proved by inoculation of bacteria-free cultures; of 29 women, 9 became infected and 7 showed symptoms after incubation periods of 5 to 20 days.

Bland, Wenrich, and Goldstein in a series of 250 cases found a significantly higher morbidity rate in childbirth in infected than in uninfected women, and they think that pregnant women with obvious infections should be treated and, if possible, freed of the parasites in the prenatal period.

Karnaky believes that *T. vaginalis* infections are associated with a lowered acidity of the vagina, along with a thinner epithelium and less glycogen in the cells. The normal high acidity of the mature human vagina is due to the presence of a flourishing culture of Döderlèin bacilli, which are probably identical with *Bacillus acidophilus*. The vagina, however, is not highly acid in children. Since *T. vaginalis* does not thrive in a normally acid vagina, treatment involves efforts to restore the acidity as well as to kill the organisms. For this purpose douches of dilute vinegar, powders containing boric acid, or acid creams or jellies have been found useful, and also application of lactose to stimulate the growth of the acid-producing bacteria, with or without cultures of *Lactobacillus*. Frequently these methods alone are sufficient.

Drugs found useful for killing the trichomonads include the arsenic and iodine compounds used against amebas, Argyrol (an organic silver compound), or, more recently, the antibiotics Aureomycin and Terramycin. The Terramycin is given in vaginal suppositories with addition of parasepts to prevent complicating fungous infections. The other drugs, mixed with kaolin or cornstarch, are given as insufflations after drying out the vagina, or in gelatin capsules inserted high up. Male infections are best treated by Carbarsone by mouth—0.25 gram 3 times a day for 7 to 10 days—together with urethral instillations of 1:3000 acriflavine twice a week. Systemic treatment of vaginal infections have not proved very successful.

Trichomonas tenax. This form of *Trichomonas* (Fig. 19B) resembles *T. vaginalis* very closely in most respects, but is smaller, usually only 6 to 10 μ in length. The nucleus has much more chromatin and often stains almost solid black, and the granules in the cytoplasm are scattered and less conspicuous. Formerly this was regarded as a rather uncommon parasite, but Hinshaw, using cultural methods, found it in 40 per cent of the people whom he examined who were above 30 years of age, but most of these had pyorrheic conditions. Beatman (1933) found it in more than 22 per cent of 350 examinations of adults in

Philadelphia: 26.5 per cent in diseased mouths and 11.4 per cent in apparently normal mouths. It is probably this species which is occasionally found in bronchial and pulmonary infections. The same or similar forms are found in the mouths of monkeys and also dogs.

Although this parasite has been found suspiciously associated with advanced inflammatory pyorrhea, its pathogenicity has not yet been proved. Along with *Entamoeba gingivalis* (see p. 105) it may well play some role, even if a minor one, in this disease. There are no special means of treatment or prevention of this parasite; only oral cleanliness is of any value.

Intestinal Trichomonads. The question of whether there is more than one species of *Trichomonas* inhabiting the human intestine has not yet been settled to the satisfaction of all, but most parasitologists are now coming to the view that there is only one, *Trichomonas* (or *Pentatrichomonas*) *hominis*, which usually, if not always, has five anterior flagella.

T. hominis (Fig. 19C) is easily separable from *T. vaginalis* and *T. tenax* by the fact that the undulating membrane extends the full length of the body, the flagellum along its margin continuing free at the posterior end. The parabasal apparatus and chromatic granules are not usually in evidence, but there is a distinct cytostome and the body commonly contains food vacuoles. In size this species is intermediate, being commonly 8 to 12 μ in length.

T. hominis occurs in a rather low percentage of people in temperate climates, but may affect 10 per cent or more of children in the tropics. Although the pathogenicity of *T. hominis* has not been proved to the satisfaction of all, the infection is often associated with persistent diarrhea, for which some investigators believe it responsible. Kessel in 1928 reported pathogenic effects in naturally and artificially infected kittens in China, but Hegner and Eskridge failed to confirm this in experiments in the United States. Hegner (1924) found that a diet rich in carbohydrates favored an abundance of intestinal trichomonads in rats, whereas a protein diet inhibited them. Ratcliffe (1928) concluded that the number of *Trichomonas* was inversely proportional to the abundance of proteolytic anaerobic bacteria, which are favored by a protein diet. Flagellate infections do not exist in strictly carnivorous animals, whereas they are abundant in herbivorous ones, and also occur in omnivorous ones.

Trichomonads in Domestic Animals. Three important *Trichomonas* infections occur among domestic animals. *Trichomonas foetus* (Fig. 20A) is a world-wide common and injurious parasite in the genital tract of cattle; it can be experimentally established in sheep also. It

is a venereal disease, transmitted from infected bulls to heifers, in which it attacks the mucous membrane of the vagina and invades the uterus, causing abortions, stillbirths, delayed conceptions, and other damage. After a number of months the animals overcome the disease and are immune to further infection. Bulls are usually infected in the preputial cavity and remain infected for life. Morgan in 1947 reported promise in the treatment of bulls with sodium iodide, but it has unpleasant effects, and after several injections both the bulls and the owners

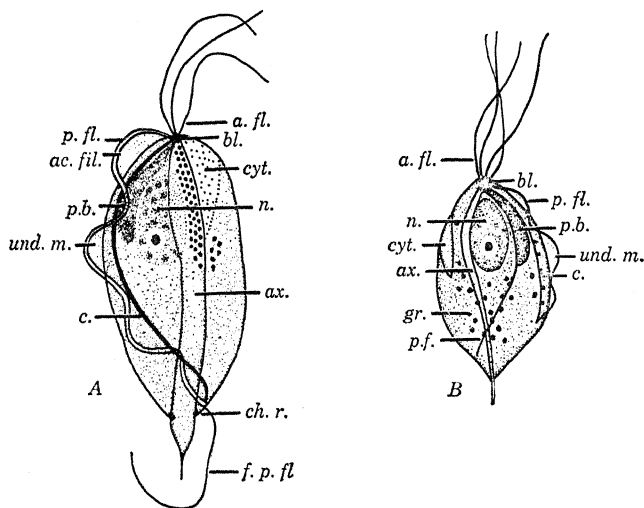


FIG. 20. *A*, *Trichomonas (Tritrichomonas) foetus* of cattle; *B*, *T. gallinae* of pigeons and other birds. Abbreviations: *ac.fil.*, accessory filament; *a.fl.*, anterior flagella; *ax.*, axostyle; *bl.*, blepharoplast; *c.*, costa; *ch.r.*, chromatic ring; *cyt.*, cytostome; *f.p.fl.*, free posterior flagellum; *gr.*, metachromatic granules; *n.*, nucleus; *p.b.*, parabasal body; *p.f.*, parabasal fibril; *p.fl.*, posterior flagellum; *und.m.*, undulating membrane. (*A* after Wenrich and Emmerson, *J. Morphol.*, 1933. *B* after Stabler, *J. Morphol.*, 1941.)

are uncooperative, so other chemotherapeutic agents are being tested. In Europe considerable success has attended the spraying and injection of the prepuce with 3 per cent H_2O_2 with a wetting agent. Three treatments at weekly intervals are said to cure most *Trichomonas foetus* infections.

Trichomonas gallinae of young pigeons and other birds (Fig. 20*B*) attacks the mucous membranes of the throat region and esophagus, and occasionally of ducts in the liver and pancreas, and causes a considerable mortality. Pigeons are ideal hosts for this parasite, since they feed their squabs by regurgitation of "pigeon milk" and transfer the parasites at the same time. Many other birds are susceptible, but

chickens and pheasants are usually refractory. In an active state the infection causes caseation and necrosis of tissues in the mouth and throat and is called "canker." Birds which do not die continue to harbor the organisms for a long time. Stabler (1947) found a wide variation in the virulence of different strains in pigeons and obtained a high degree of immunity to severe strains by inoculation with relatively harmless ones. Enheptin, a nitrothiazole, was shown by Stabler and Mellentin (see Stabler, 1954) to be very effective in treatment.

T. gallinarum affects the lower digestive tract of galliform birds but is especially injurious to turkeys. The parasite affects particularly the liver and ceca. It causes droopiness and liquid yellow droppings, and is often fatal to young turkeys. A 1 : 2000 solution of copper sulfate substituted for drinking water for 2 or 3 days is said to be helpful in treatment.

Spindler, Shorb, and Hill (1953) have found evidence that a disease of the nose of pigs, called atrophic rhinitis, is due to infection by a species of *Trichomonas*, which has also been found in the iliocecal region of the intestine.

Chilomastix mesnili

This organism, often confused with *Trichomonas* by careless observers, inhabits the large intestine of about 3 to 10 per cent or more of human beings; in Egyptian villages the writer found 13 per cent infection. Closely similar forms are found in all groups of vertebrates. They are common in both rats and frogs. *Chilomastix* (Fig. 21) is an unsymmetrical, pear-shaped animal which has its posterior end drawn out into a sharply pointed tail. It varies in length from 6 to 20 μ , but the usual length is 10 to 15 μ . The body is less plastic than in *Trichomonas*, so there is less variability in shape. It has three slender anterior flagella which, like those of *Trichomonas*, function as two groups, two of them lashing back against the left side of the body, and one against the right. The relatively enormous cytostome is an oval groove half or more the length of the body, the lips of which are supported by a complicated system of fibers. Lying in this

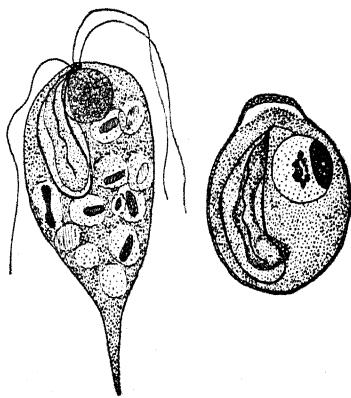


FIG. 21. *Chilomastix mesnili*. Left, trophozoite; right, cyst. $\times 3000$. (After Boeck, J. *Expl. Med.*, 1921.)

groove is a fourth flagellum, attached to the left lip by an undulating membrane. By its flickering movements this "tongue" wafts food particles into the depths of the groove, where they pass into the body to be enclosed in food vacuoles, with which the body is often literally crammed. The nucleus lies in the fore part of the body just behind the free flagella.

The animals do not move as rapidly as *Trichomonas*, but proceed by a sort of jerky spiral movement unlike the continuous wobbly progression of *Trichomonas*.

The ordinary multiplication is by simple fission, but sometimes large multinucleate forms are produced. Unlike *Trichomonas*, *Chilomastix* forms lemon-shaped cysts, narrower at the anterior end. The cysts are usually about 7 to 9 μ long; they have thin walls except where thickened at the anterior end, and the fibers of the cytostome, practically unaltered in form, lie alongside of or overlapping the nucleus. Occasionally the nuclei and cytostomal fibers are duplicated in the cysts, which then presumably give rise to two individuals when they hatch. The cysts are very resistant and live for months in water at room temperature, and for several days in the intestine of flies. Boeck found that a temperature of 72°C. was necessary to kill them.

There is little evidence that *Chilomastix* is pathogenic. Westphal (1939), in experiments on himself, found this parasite and also *Enteromonas hominis* to fluctuate with the condition of the intestine, and considers their presence a result rather than the cause of intestinal ailments with which they may be associated.

Giardia

Giardia (Fig. 22), once known as *Lamblia*, contains flagellates which are remarkable in a number of ways. They are odd-looking creatures, which have their nuclei and other organelles reduplicated like closely bound Siamese twins. They inhabit the upper part of the small intestine instead of the large intestine favored by all the other intestinal Protozoa; they attach themselves to the surface of the mucosal cells where they presumably absorb nourishment directly from the host. They have such close specificity that one recent writer on them (Ansari, 1952) thinks that when one species is found in more than one kind of animal, it is only because it was a parasite of a common ancestor from which the present-day hosts evolved, the parasites having undergone evolution more slowly than the hosts. They are the only intestinal Protozoa which cannot be cultured in artificial media. They inhabit the intestines of all kinds of vertebrates from fish to man; Ansari (1952) listed 38 named and described species, as well as 8 or 10 others non-committally referred to as "*Giardia* sp."

The species found in man, usually called *G. lamblia* by American

writers and *G. intestinalis* in Europe, is also reported from both Old and New World monkeys. It is hard to go along with Ansari's idea that this single species has failed to undergo any evolutionary change since the millions of years ago when these groups of Primates began their evolution, so we must assume either that the monkey strains are not actually identical with the human ones, or that the parasites have enough adaptability to pass from one Primate species to another.

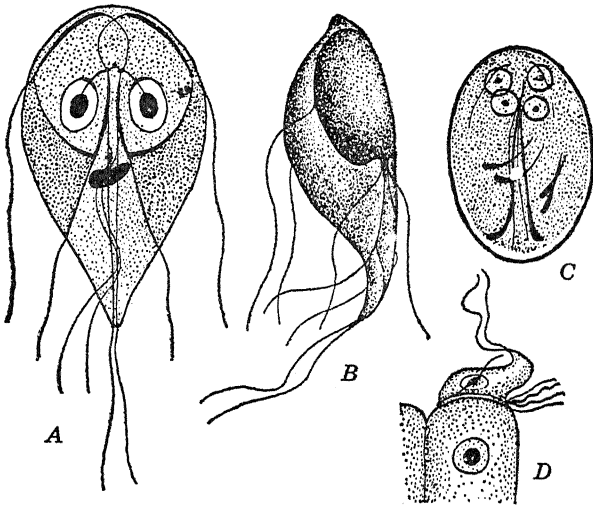


FIG. 22. *Giardia lamblia*. A, face view of trophozoite; B, semiprofile view; C, cyst; D, position of trophozoite resting on epithelial cell. A, B, and C, $\times 3000$; D, $\times 1000$. (A, after Simon, *Am. J. Hyg.*, 1921; B and D, after Grassi and Schewiakoff, *Ztschr. Wissensch. Zool.*, 1888; C, original.)

Morphology. In appearance *Giardia* is a fantastic little animal. It is bilaterally symmetrical, with two nuclei analogous to a pair of *Chilomastix*-like flagellates fused together in the middle line. A dead giardia trophozoite gives the impression of a wizened monkey face looking up at you. The outline of the body is strikingly like that of a tennis racket without the handle. In side view it is shaped like a pear split lengthwise in two parts, with the flat surface in the broadest part gouged out as a large concave sucking disc, with slightly raised margins. The finely tapering posterior end is usually turned up over the convex back. There are eight flagella, arranged as shown in Fig. 22. They may be thought of as corresponding more or less to eyebrows, moustaches, and beard. The body is 8 to 16 μ in length by 5 to 12 μ in width, the mean being about 12 by 8.5 μ . There appear to be two races which differ in size and in shape of the parabasal body.

The two nuclei have large central endosomes. Between them are

two slender rods, the axostyles, to which the nuclei are anchored by slender fibrils. There is a complicated system of basal granules and fibrils connecting with the flagella and the rods supporting the sucking disc, as shown in Fig. 22A. Just behind the disc is a deep-staining parabasal body, often giving the appearance of two bodies fused together. The cysts (Fig. 22C) are thick-walled and oval and about 8 to 14 μ in length, commonly about 10 μ . Incomplete division takes place in the cyst; when mature the cyst usually contains 4 nuclei, either clustered at one end or lying in pairs at opposite poles, and it also shows deep-staining axostyles and fibrils lying diagonally in the cyst, and 2 or 4 curved parabasals.

Biology. As already noted, *Giardia* makes its home in the small intestine, especially in the duodenum, occasionally invading bile ducts, etc. It frequently develops in the large intestine in dogs infected via the rectum. Hegner, however, found giardias of both rat and human origin to localize only in the upper part of the small intestine of rats, and showed that they were attracted by bile salts. Although *Giardia* infections are found in people of all ages, they are commoner in children. In Egyptian villages, where there is constant exposure to infection, the writer (Chandler, 1954) found this parasite in 16 per cent of people below the age of puberty and in only 3 per cent of those above. On the other hand, Rendtorff (1954) was able to infect 100 per cent of adult men in the United States when 100 or more cysts were fed, although most of the infections were very light, and all of them disappeared spontaneously, usually within 1 to 6 weeks. A possible explanation for these apparently discordant results is that the parasites stimulate some degree of resistance; this allows new infections to become established only infrequently when there is constant exposure, but otherwise it wears off and allows new infections to develop which last until the resistance is restimulated.

In life these grotesque little creatures fasten themselves by their hollow faces to the convex surfaces of epithelial cells in the small intestine, their flagella streaming like the barbels of a catfish (Fig. 22D). Sometimes large areas of epithelium are practically covered with them, each one perched on a separate cell. Their vast numbers can be judged from the fact that in one instance Miss Porter estimated the number of cysts in a single stool to exceed 14,000,000,000. The number of cysts in an average stool in a case of moderate infection she estimated at over 300,000,000. The motile forms are not normally found in the stools, but in cases of diarrhea dead ones may be present in considerable numbers. They do not ingest solid food, nor do they appear to dissolve tissue cells; possibly they feed on the abundant

secretion of mucus which their presence stimulates, and on a variety of amino acids, vitamins, and other substances which are constantly passing in and out of the intestinal mucosal cells (see Read, 1950).

Multiplication occurs by division into two in a plane parallel with the broad surfaces, and occasionally multiple fission occurs as in other intestinal flagellates. The cysts are formed intermittently; enormous numbers may be found on one day and then none for several days, when a shower of them again appears. Occasionally fecal examination fails to reveal them even when they are present in the duodenum in large numbers. The cysts remain alive in feces for 10 days or more and survive many days in the gut of roaches. The parasite is a very persistent one; infections sometimes last for many years, possibly in some cases for life.

Pathogenicity. There is no longer any doubt of the pathogenicity of *Giardia*. Véghelyi in 1939 found evidence of mechanical interference with absorption, particularly of fats, from the intestine by the layer of parasites adhering to its wall. It is obvious that this might lead to vitamin deficiencies, particularly of the fat-soluble ones. The presence of large amounts of unabsorbed fats in the stools causes a persistent or recurring diarrhea, often with large amounts of yellow mucus. The symptoms may resemble those of celiac disease, sprue, or chronic gall bladder disease. Epigastric pains, vague abdominal discomfort, loss of appetite, apathy, headache, etc., may be present. In many cases, on the other hand, there are no evident symptoms. Occasionally the parasites are found in the bile ducts and even in the gall bladder. It is possible that they may cause some irritation in the bile ducts and predispose them to chronic infection, but the evidence for this is inconclusive.

Giardia infections are very susceptible to the anti-malarial drugs, atebirin and Chloroquin, given at the rate of 0.1 gram three times a day for about 5 days. Cysts cease to be passed after the second, or third day. One *Giardia*-infected young man whom the writer treated with atebirin was extremely ill, had had no appetite for weeks, and was very emaciated. After treatment he recovered his appetite within 24 hours, gained several pounds in a week, and was restored to normal health in a month.

Other Intestinal Flagellates

A few other flagellates may be residents of the human intestine, but they are relatively rare and of little importance.

***Retortamonas intestinalis*.** This little slipper-shaped animal, formerly called *Embadomonas intestinalis*, though rare, has been found

in many parts of the world. The fact that members of the same genus occur in various insects, especially aquatic ones, and in frogs and turtles, suggests that the infections of man and other mammals in which they have been found may perhaps be derived from the swallowing of cysts of some insect or aquatic species with water. Its rarity makes it doubtful that it is normally a human parasite. It is very small, only 4 to 9 μ long by 3 to 4 μ in breadth; it has two flagella, a long, slender anterior one and a shorter, thicker one which lies partly in the large elongated cytostome, the borders of which have supporting fibers (Fig. 23A and B). The nucleus is anterior in posi-

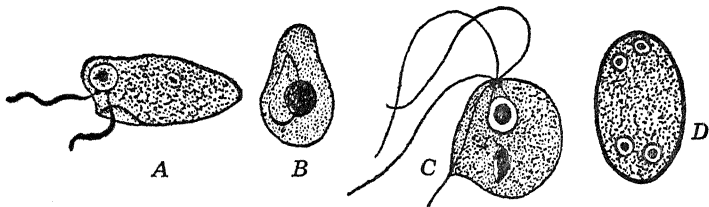


FIG. 23. A and B, *Retortamonas* (= *Embadomonas*) *intestinalis*, trophozoite and cyst; C and D, *Enteromonas* (= *Tricercomonas*) *intestinalis*. $\times 3000$. (After Wenyon and O'Connor, 1917.)

tion. The cysts are whitish, opalescent, pear-shaped bodies, 4.5 to 6 or 7 μ long when living. When stained they show what appears to be the endosome of the nucleus, sometimes dumbbell-shaped, and fibers which Wenyon interprets as the marginal fibers of the cytostome.

Faust described another species, *R. sinensis*, from China; it is larger and is said to have the two flagella alike, but Wenyon believes it to be identical with *R. intestinalis*. It was found in nine cases with diarrheic stools, and was again reported from two cases in China by Watt in 1933. It has been successfully cultivated, and seems to be a valid species.

***Enteromonas hominis*.** This flagellate (Fig. 23C and D) which is believed by Dobell to be identical with another flagellate reported from man, *Tricercomonas intestinalis*, is an extremely small oval or pear-shaped organism, 4 to 10 μ long by 3 to 6 μ broad, slightly flattened on one side, where a flagellum is attached until it becomes free at the posterior end. There is also a cluster of three anterior flagella. Small oval cysts 6 to 8 μ long are formed which have well-developed cyst walls, giving them a double outline, and one to four nuclei, visible only when stained. In cysts with two or four nuclei these are arranged at opposite ends. The parasite has been reported from many parts of the world, but is usually considered rare. In an Egyptian village Lawless (personal communication) found it in 74 per cent of 100

people, 80 of whom were examined six times over a period of 30 months, and Kessel et al. found 20 per cent incidence in Tahiti. Its small size makes it very easily overlooked even if searched for with a high-dry lens. There is no evidence that it is pathogenic, and infections sometimes persist only for a short time.

Intestinal Flagellates of Domestic Animals

Although all species of vertebrate animals are probably parasitized by a number of species of flagellates, pathogenic effects are produced in only a few cases. Certain species of *Trichomonas* (see pp. 119–120) are exceptions. *Giardia* has been reported as sometimes causing severe damage to rabbits and dogs, and the writer has seen dogs with intermittent attacks of diarrhea of the type associated with *Giardia* infections. Other important flagellates are *Histomonas meleagridis* and *Hexamita* spp.

***Histomonas meleagridis*.** This important parasite of galliform birds (Fig. 24A, B, C) causes infectious enterohepatitis or "blackhead" in turkeys. It is found in both the ceca and the liver, and occasionally in the kidney and spleen. It is an ameboid organism 8 to 10 μ in

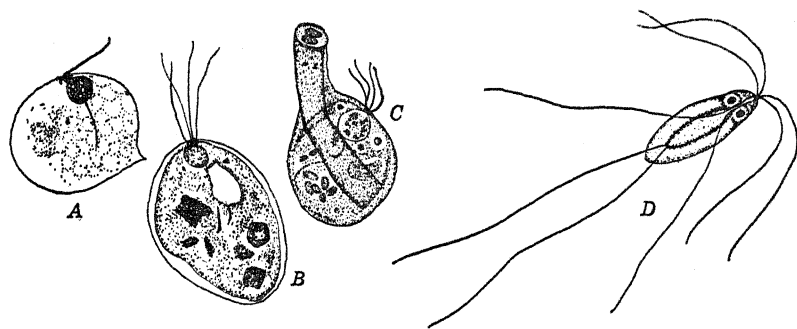


FIG. 24. A–C, *Histomonas meleagridis*: A, tissue form with one flagellum and cytoplasmic fibril; B, lumen form with four flagella; C, lumen form with cytoplasmic process engulfing bacteria. D, *Hexamita meleagridis*. (A and B, after Tyzzer, *Proc. Am. Acad. Arts Sci.*, 69, 1934; C, after Wenrich, *J. Morphol.*, 72, 1943; D, after McNeil, Hinshaw, and Kofoid, *Am. J. Hyg.*, 34, 1941.)

diameter, with a small eccentric nucleus with a blepharoplast on or near the nuclear membrane. From this arise one to four flagella in the intestinal forms, often, however, not extending beyond the cell wall. Organisms in the tissues have no flagella. The organism fails to produce cysts and lives for a very short time when passed in the droppings, which do not cause infection when swallowed. The organism has, however, a very clever means of transfer to a new host by becoming

enclosed inside the egg shells of cecal worms, *Heterakis* (see p. 448). When embryonated eggs of *Heterakis* are fed to turkey poults a high mortality from blackhead results. In nature, turkeys are infected by worm eggs passed from healthy chicken carriers; this is the principal reason why it is usually disastrous to try to raise chickens and turkeys together. The disease can be induced experimentally by rectal injection of infected material; the ceca are first attacked, and then the parasite migrates to the liver by way of the blood stream (Farmer et al., 1951). A nitrothiazole, called Enheptin T, when mixed with food at 0.05 per cent, is a highly effective prophylactic, and is curative at 0.1 per cent (see Horton-Smith and Long, 1951).

***Hexamita* spp.** A number of species of *Hexamita* occur in various vertebrates. They are more or less elongated flagellates with two anterior nuclei, four anterior flagella in pairs, and two which arise anteriorly but pass posteriorly through the body to emerge near the posterior end (Fig. 24D). These parasites cause a severe diarrhea in young turkeys and pigeons. Quail, partridges, and chicks suffer less. According to McNeil, Hinshaw, and Kofoed (1941), *H. meleagridis* of turkeys and *H. columbae* of other birds are two distinct species. *H. columbae* was not transferable to turkeys, and *H. meleagridis* caused only temporary infections in chickens and ducks.

INTESTINAL CILIATES

All the intestinal ciliates of warm-blooded animals belong to the subclass Euciliatia (see p. 42). Amphibia, on the other hand, have the rectum inhabited by many species of Opalinidae, which belong in the subclass Protociliatia.

The Euciliatia are classified as follows:

Order 1. **Holotrichida.** No adoral zone of flattened cilia or membranelles. Includes *Paramecium* and many coprozoic ciliates, but no parasites of higher vertebrates.

Order 2. **Spirotrichida.** Adoral zone of membranelles winding clockwise to cytostome, the peristome (mouth region) not protruded. Two suborders contain parasites of vertebrates: **Heterotrichina**, with body covered with cilia, includes *Balantidium*; **Oligotrichina**, with body nonciliated, but with adoral and other zones of membranelles, includes numerous species in stomach of ruminants and colon of horses.

Order 3. **Chonotrichida.** Like order 2, but peristome protruding like a funnel. No vertebrate parasites.

Order 4. **Peritrichida.** Body not entirely ciliated; anterior region disc-like with counterclockwise adoral zone of membranelles. Example, *Vorticella*. None parasitic in vertebrates.

The stomachs of ruminants and the large intestine of horses harbor numerous species of commensal ciliates belonging to the suborder

Oligotrichina. They may play some part in the digestion of cellulose in these animals. One of the species from ruminants is shown in Fig. 1.

***Balantidium coli*.** This is a parasite of the large intestine of man, monkeys, and pigs. A parasite in rats identical with *B. coli* was reported from Moscow; and rats can be experimentally infected. McDonald, in 1922, believed that the pig harbors another species, a *B. suis*, which is not infective for man, but Hegner, in 1934, doubted this.

B. coli (Fig. 25), as found in man, is much larger than any of the other protozoan inhabitants of the human intestine and usually measures 50 to 80 μ in length, with a breadth between two-thirds and

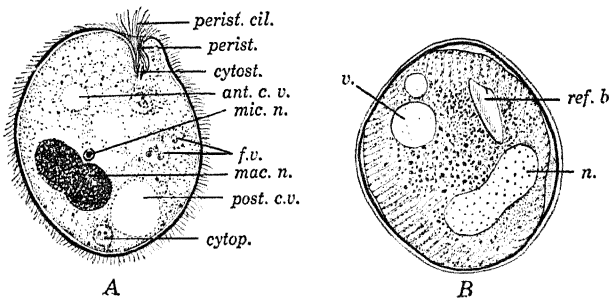


FIG. 25. *Balantidium coli*: A, trophozoite; ant.c.v., anterior contractile vacuole; cytot., cytostome; cytop., cytophyge; f.v., food vacuoles; mac.n., macronucleus; mic.n., micronucleus; perist., peristome; perist.cil., peristomal cilia; post.c.v., posterior contractile vacuole. B, cyst; n., macronucleus; ref.b., refractile body; v., vacuole. About $\times 500$. (A, original; B, adapted from Dobell and O'Connor, *Intestinal Protozoa of Man*, 1921.)

three-fourths as great. In pigs it sometimes reaches a length of 200 μ . It is shaped like an egg or pear, and has at the anterior end an obliquely arranged depression, the peristome, which may appear wide open or slit-like, and in the bottom of which is the cytostome. The whole body is covered with fine cilia arranged in rows, with a special row of longer "adoral" cilia surrounding the peristome. The macronucleus is only very slightly curved, usually with a slight concavity on either side. It usually lies obliquely near the middle of the body and is about two-fifths the length of the body. The micronucleus is very small and inconspicuous. There are two contractile vacuoles, and food vacuoles circulate in the endoplasm. Like other ciliates, *Balantidium* divides by transverse fission, a new cytostome being formed by the posterior daughter.

A process of conjugation occurs, similar in its general features to that of *Paramecium*. Thick-walled cysts are formed in which single individuals are usually enclosed. Slow-moving cilia are at first visible on

encysted ciliates, but later all structures except the nuclei and sometimes one or more refractile bodies disappear. No multiplication takes place in the cysts.

Pigs are usually regarded as important sources of human infection. Such infections are rather infrequently reported, but they may be locally common. Young (1939) reported 7 cases, all with marked diarrhea, among 142 insane hospital patients examined in South Carolina. Among 3000 Puerto Ricans in New York, 20 cases were found (Shookhoff, 1951) whereas in Puerto Rico there is about twice that incidence. Of the 20 cases in New York, all in children, 18 had a history of contact with pigs. Apparently large or repeated doses of cysts or special susceptibility is necessary for human infection, for Young, using moderate numbers of parasites, was unable to produce infection experimentally in two volunteers. Large inocula are also necessary to get cultures going.

In man *B. coli* is known to be a pathogenic parasite, though in pigs it appears to be harmless. In man it may cause ulceration of the large intestine and invade the tissues of the walls; the colon is sometimes ulcerated from end to end. Nevertheless, the majority of cases suffer only from diarrhea and may show no symptoms at all; only a small number develop severe or fatal dysentery. In the 20 Puerto Rican cases in New York, 10 admitted having symptoms (diarrhea or dysentery) but probably more did, for many people in the tropics consider diarrhea more or less a normal part of life, as indeed it is if universality constitutes normality.

Ciliates of the genus *Nyctotherus* have on rare occasions been recorded from human feces, but it is probably coprophagous (see Wichterman, 1938). Like amebas and flagellates, coprozoic ciliates are common and have misled more than one parasitologist.

Balantidium infections have been treated with varying success with some anti-amebic drugs, particularly Carbarsone, but there is now evidence that Aureomycin and Terramycin are very effective. These antibiotics are given for 10 to 15 days, the total dosage being from 7 to 28 grams. The ciliates disappear within 2 to 4 days, and no relapses occur for at least 2 weeks or so after treatment.

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Hemoflagellates

I. *Leishmania* and Leishmaniasis

The Trypanosomidae

The term "hemoflagellates" is used for those flagellates which habitually live in the blood or tissues of man or other animals. There are only two kinds of these which occur in man, namely, the leishman bodies, belonging to the genus *Leishmania*, and the trypanosomes, belonging to the genus *Trypanosoma*. These two types of organisms, however, are only two of a number of genera which all belong to one family, Trypanosomidae, in the order Protomastigida (see p. 111). Other members of the family occur as gut parasites of insects or lizards, and still others as parasites of plants. Since both the hemoflagellates and the plant parasites undergo cycles of development in the gut of insects, it is safe to presume that this entire group of flagellates was originally and primitively parasitic in the gut of insects.

Four distinct morphological types of these parasites are found in the bodies of insects:

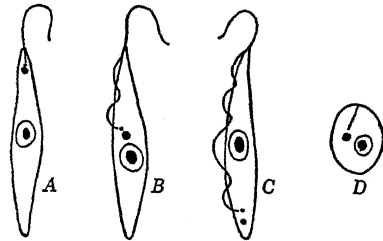


FIG. 26. Diagram of forms assumed by Trypanosomidae either as adults or as developmental forms. A, Leptomonas; B, Crithidia; C, Trypanosoma; D, Leishmania. (After Wenyon, Protozoology, 1926.)

1. The leptomonas type (Fig. 26A). This is the most primitive type, in which the body is more or less elongate or pear shaped: it contains a nucleus near the center, a kinetoplast near the anterior end, and a single long slender flagellum which arises from a basal granule closely associated with the kinetoplast. All the other types of Trypanosomidae may be considered as having arisen from this.

2. The crithidia type (Fig. 26B). This differs in that the flagellum

arises from a kinetoplast which has shifted back to a position just in front of the nucleus and is connected with the body, up to the anterior end, by an undulating membrane.

3. The trypanosoma type (Fig. 26C). In this the kinetoplast has moved far behind the nucleus to a point near the posterior end of the body, and the flagellum is attached to the body for most of its length, with or without an undulating membrane.

4. The leishmania type (Fig. 26D). This is a rounded-up form which contains a nucleus and a kinetoplast, but is entirely devoid of a flagellum. Any of the other three types may assume this form and, conversely, may be developed out of it.

Any or all of these forms may occur in the digestive tracts of insects, but only the leishmania and trypanosome forms occur in the blood of vertebrates.

The fact that some flagellates never develop farther than the leptomonas form, and others never, so far as known at present, farther than the crithidia form, whereas the trypanosomes go through all the stages, makes a study of this group of flagellates very confusing. When a leptomonas or crithidia type is found in an insect gut, it is impossible to say, without further investigation, whether it is an adult animal which never undergoes any further development, or is only a developmental phase of a trypanosome of a vertebrate animal. A number of crithidias which were supposed to be purely insect parasites with no trypanosome stage have been found to develop into trypanosomes in the blood of certain vertebrates, so it may be that most of the crithidias are really developmental stages of these parasites.

The Trypanosomidae are divided into a number of genera on the basis of the morphological forms they assume and on whether they are transmissible to vertebrate animals or to plants. The following genera are usually recognized:

1. Genus *Leptomonas*. Species having only leptomonas and leishmania stages, and confined to invertebrate hosts. They are common in various kinds of bugs, larvae and adults of fleas, various Diptera, and other insects. They live in the hindgut, where they attach themselves to the epithelial cells by their flagellar ends, the free flagella being very short or lacking (Fig. 27). Often they occur in rosettes of dozens of individuals. They produce resistant cyst-like forms resembling ordinary leishmania forms but apparently protected by cyst walls.

2. Genus *Leishmania*. Species having only leptomonas and leishmania stages, but transmissible to vertebrates. Unlike *Leptomonas*, they develop mainly in the stomach and foregut, and form no resistant cyst-like bodies. In vertebrates they develop intracellularly and entirely in the leishmania phase, except one species, *Leishmania chameleonis*, which retains the leptomonas form in the intestine of lizards. In artificial cultures or in insects they assume the leptomonas form and are extracellular.

3. Genus *Phytomonas*. Similar to *Leptomonas*, but transmitted to plants, particularly *Euphorbia* and milkweeds, where they multiply in the latex. In some, at least, the organisms are said to be inoculated by the bites of insects, and cyst-like forms are not found in the feces.

4. Genus *Crithidia*. Strictly insect parasites in which leptomonas, leishmania, and crithidia stages occur, and in which cyst-like forms are voided in the feces of the host. As noted above, many of these have proved to be developmental stages of trypanosomes.

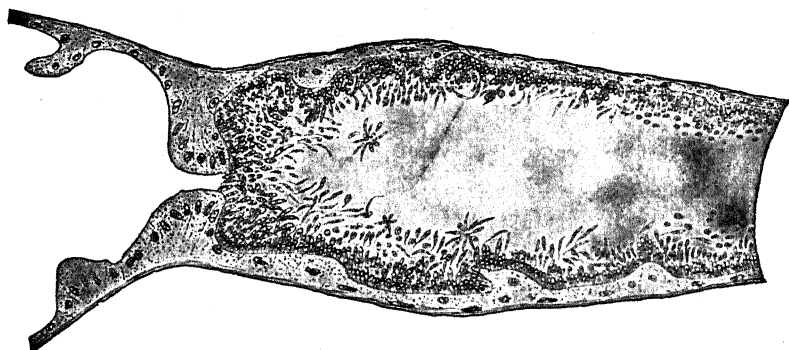


FIG. 27. Longitudinal section of the intestine of a dog flea, showing leptomonads lining the hindgut. $\times 170$. (After Wenyon, *Protozoology*, 1926.)

5. Genus *Herpetomonas*. Strictly insect parasites having leptomonas, leishmania, and crithidia stages, and also a stage in which the kinetoplast is at the posterior end of the body as in trypanosomes, but with the flagellum passing along the body like a rhizoplast, instead of being attached to an undulating membrane as in true trypanosomes. Cyst-like forms are produced in the feces of the host (Fig. 27).

6. Genus *Trypanosoma*. Species which have both vertebrate and invertebrate hosts, and may go through all the stages of development. Some of the more primitive forms, e.g., *Trypanosoma cruzi* and *T. lewisi*, have both trypanosome and leishmania forms (the latter intracellular) in their vertebrate hosts, and may go through all the phases in the invertebrate hosts, where they multiply in the hindgut like typical insect flagellates. More specialized ones, e.g., the African species transmitted by tsetse flies, occur exclusively in the trypanosome form in their vertebrate hosts, free in the blood and lymph, and may exist only in the crithidia and trypanosome forms in their insect hosts, where they develop in anterior parts of the digestive system (see Fig. 30).

Leishman Bodies and Leishmaniasis

In the tissues of mammals parasites of the genus *Leishmania* invade cells and multiply in them, particularly cells of the reticulo-endothelial system in the skin, mucosa, lymph nodes, spleen, liver, bone marrow, etc. They are taken up by leucocytes, especially large mononuclears, and thus enter the blood stream. They are very small, round or oval

bodies, usually about 1.5 to 4 μ in diameter, possessing a round nucleus and a dot- or rod-shaped kinetoplast which stain well with Giemsa or related stains (Fig. 28). Torpedo-shaped forms are sometimes seen. Inside the cells the organisms multiply by simple fission, producing large clusters of 50 to 200 parasites, which distend and finally rupture

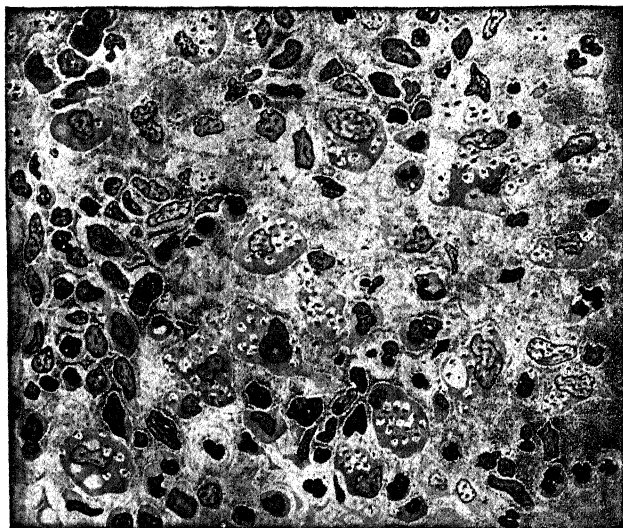


FIG. 28. Section of human spleen showing numerous leishman bodies in the cells. $\times 750$. (After Nattan-Larrier, from Wenyon, *Protozoology*, 1926.)

the cells, setting the minute parasites free to invade, or be taken up by, other cells. They may also pass from cell to cell along protoplasmic processes. This parasitization of cells of the reticulo-endothelial system is an interesting reversal of the usual course of events. The parasites are probably picked up by these cells with phagocytic intent, but instead of being digested they grow and multiply, and ultimately destroy the would-be destroyer.

Cultural Forms. The parasites develop readily in cultures containing blood, when kept at room temperatures. In such cultures they transform into active, flagellated leptomonas forms (Fig. 29). Typically these are spindle shaped, 14 to 20 μ long and 1.5 to 3.5 μ broad. The flagellum is as long as, or longer than, the body. The round or oval nucleus is near the center of the body, and the oval kinetoplast lies transversely near the anterior end. Division is by longitudinal fission; sometimes rosette clusters develop. In young cultures many stumpy, pear-shaped, or oval forms are found, but longer and more slender forms predominate later.

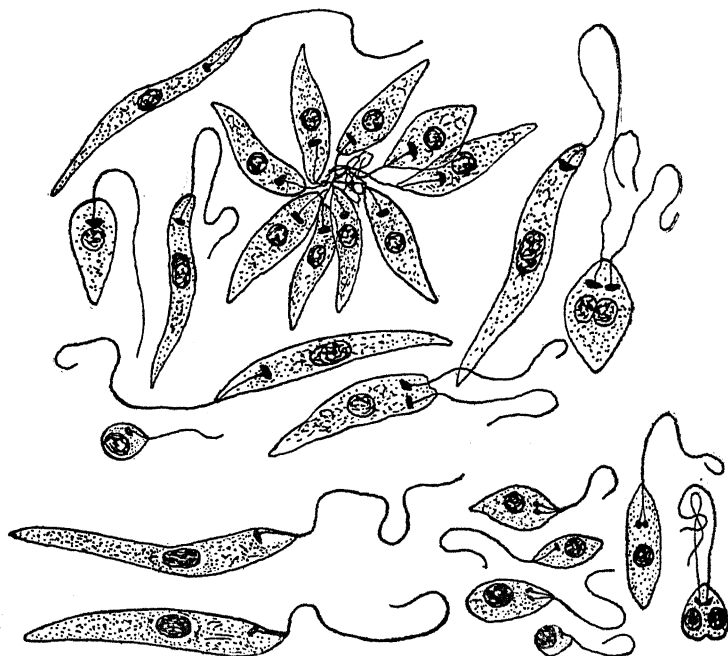


FIG. 29. *Leishmania donovani*. Upper figures, forms seen in cultures (original.) Lower figures, forms found in midgut of *Phlebotomus argentipes*; at left, forms found in lumen; at right, forms found attached to walls. $\times 1600$. (Sketched from figures by Shortt, Barraud, and Craighead, *Ind. J. Med. Research*, 1926.)

Development in Insects and Transmission. When ingested by certain insects the parasites undergo development into leptomonas forms just as they do in cultures, and may produce leishmania forms also. This development was first observed by Patton in India (1907) to occur in bedbugs fed on kala-azar patients. This was an unfortunate discovery, since it started investigators on a false trail in search for the transmitting agent and led to more than a dozen years of futile work. As a matter of fact, few problems in parasitology have caused more fruitless effort, more blasted hopes, more false conclusions, or more unfounded speculation than the transmission of leishmaniasis; it was not until 1942 that the final piece was fitted into the puzzle. Shortt and his colleagues of the Indian Kala-azar Commission finally concluded, in 1925, that the bedbug had nothing to do with the transmission in spite of development of the flagellates in its gut, as any careful observer of the epidemiology might have guessed. In the Mediterranean region fleas were strongly suspected since they fed on in-

fected dogs and were found to harbor leptomonads; these were finally shown to be species of *Leptomonas* peculiar to the fleas, and the case against fleas as transmitters of leishmaniasis was thrown out of court by Nicolle and Anderson in 1924.

In 1921 a Kala-azar Inquiry was set up in Calcutta, and in 1924 a Kala-azar Commission began work in Assam. Guided by an observation of Sinton's that the distribution of *Phlebotomus argentipes* in India coincides closely with that of kala-azar, Knowles, Napier, and Smith found epidemiological reasons for suspecting this sandfly as a

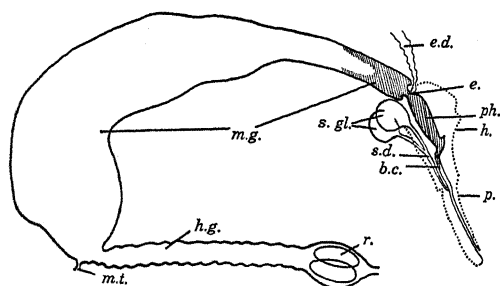


FIG. 30. Gut of sandfly, showing "blocking" of pharynx and forepart of midgut (shaded area) by *Leishmania donovani*; b.c., buccal cavity; e., esophagus; e.d., esophageal diverticulum; h., head; h.g., hindgut; m.g., midgut; m.t., Malpighian tubule; p., proboscis; ph., pharynx; r., rectum; s.d., salivary duct; s.gl., salivary glands. (After Shortt, Barraud, and Craighead, *Ind. J. Med. Research*, 1926.)

transmitter in Calcutta. In the same year, 1924, they made the important discovery that a high percentage of these flies became infected when fed on kala-azar cases. This was quickly corroborated by Christophers, Shortt, and Barraud in Assam, and soon thereafter many important details were added concerning the development of the flagellates in the sandfly, including demonstration of occasional massive infections of the pharynx and proboscis.

Then followed years of patient but largely fruitless effort to prove actual transmission by sandflies. In the course of hundreds of trials, only four successful infections were obtained, all in hamsters; transmission to human volunteers always failed. In 1939 Smith, Halder, and Ahmed made the interesting discovery that if sandflies, after an infective meal, were fed on raisins instead of additional blood meals, the flagellates frequently grew so numerous that they blocked the pharynx as do plague germs in fleas (Fig. 30). These authors then subjected five hamsters to bites of flies fed on raisins after their infective blood meal, and every one developed kala-azar; of five others fed on by flies given repeated blood meals, at least four failed to become

infected (one escaped). In confirmation of this remarkable result, Swaminath, Shortt, and Anderson (1942) then succeeded in infecting each one of five human volunteers in Assam. Thus to a successful end came 20 years of patience, perseverance, labor, and ingenuity.

This work, taken in conjunction with the epidemiology and the success of experimental infection of sandflies in various parts of the world, leaves no further doubt that sandflies are an important factor in the transmission of all forms of leishmaniasis, although other methods are also possible, e.g., by excretions of infected individuals in kala-azar, and by means of flies in the cutaneous forms of the disease.

Types of Leishmaniasis. *Leishmania* infections are usually classed in two general types, visceral and cutaneous, but there are several types of each, and intermediate conditions exist. Visceral leishmaniasis, or kala-azar, is a generalized and often fatal disease, accompanied by fever and enlargement of spleen and liver. Cutaneous leishmaniasis is limited to development of one or more local sores, usually without fever or generalized symptoms. These sores may be confined to the skin, as in Oriental sore of the Old World, or may spread to mucous membranes of the nose and mouth, as in espundia of tropical America. This mucocutaneous form of the disease is evidently caused by parasites that are intermediate in invasive power.

It is probably best to recognize only two distinct species of *Leishmania*: *L. donovani*, causing the various visceral forms of the disease; and *L. tropica*, causing the various cutaneous and mucocutaneous forms, of which several subspecies are recognized, based on clinical manifestations (see below). Possibly the vectors are different also. The parasite of the severe mucocutaneous form of the disease in Brazil (espundia) is sometimes recognized as a distinct species, *brasiliensis*, but since there are intermediate forms between this and typical *L. tropica*, all are best considered subspecies, as suggested by Biagi (1953), who gives an excellent review of the subject. The various subspecies show no constant morphological, cultural, or serological differences, nor do they show clear-cut differences in their pathogenicity for laboratory animals.

Of visceral leishmaniasis or kala-azar, Biagi (1953) recognizes five types: (1) Chinese, with some preference for children; affects dogs, and is transmitted by *Phlebotomus chinensis* and *P. sergenti*; (2) Indian, occurring chiefly in adults, does not attack dogs, and is transmitted by *P. argentipes*; (3) Mediterranean, almost confined to children, with dogs an important reservoir; transmitted by *P. perniciosus* and *P. major*; (4) Sudanese, characterized by frequent oral lesions and by unusual refractoriness to antimony treatment; and (5) South American, attack-

ing all ages, with reservoir in dogs and cats; vectors *P. intermedius* and *P. longipalpis*.

In the Old World there are two forms of cutaneous leishmaniasis, the parasites of which the Russians have designated as *L. tropica minor* and *L. t. major*, respectively: (1) Classical Oriental sore, caused by *L. t. minor*, common from the Mediterranean to central and northern India; produces circumscribed "dry" sores (Fig. 31), with abundant parasites in them; incubation several months; subject to spontaneous cure; no metastatic lesions, and no mucous membrane involvement; involvement of lymph glands in 10 per cent; dogs susceptible; urban; transmitted by *P. papatasi*, *P. sergenti*, *P. perfliewi* (in Italy) and *P. longicuspis* (in Algeria). (2) "Wet" sores, caused by *L. t. major*, with a short incubation of 1 to 6 weeks; sores quick to ulcerate; lymph glands commonly involved; no cross-immunity with Oriental sore; rural, with reservoir in wild rodents (gerbils and ground squirrels), and transmitted by *P. caucasicus*, which lives in the burrows of these rodents.

In tropical America, Biagi recognizes four types of cutaneous leishmaniasis as follows: (1) Mucocutaneous (Fig. 32A) in rain forests of Brazil; spreading, chronic, cutaneous lesions, tending to invade mucous membranes either by extension or (more often) by metastasis; much destruction of tissue; parasites relatively scarce in lesions, and deep; spontaneous recovery rare; lymph gland involvement infrequent. (2) Uta, in mountains of Peru; small, numerous skin lesions, causing little destruction of tissue; benign. (3) Leishmaniasis or "buba" or "pian bois" of Panama, Costa Rica, and the Guianas, showing moderate ulceration tending to spontaneous cure after a few years except when in the nose; mucous membrane lesions in 5 per cent, always by extension and not metastases; lymph gland involvement in 10 per cent. Floch (1954) proposed the subspecies name "*guianensis*" for this variety, and considered the parasite of uta in Peru to be the same. (4) Chiclero ulcer of Guatemala, Belize, and southeastern Mexico, characterized by small, non-destructive skin lesions which get well in a few weeks or months except when on the ear (Fig. 32B), for which the parasites have a special predilection and where they cause chronic, disfiguring, subcutaneous, nodular ulcers lasting many years; no metastasis to mucous membranes, rarely cutaneous metastases, and lymph gland involvement rare (2 per cent); parasites scanty in lesions. For this variety Biagi proposed the name *L. tropica*, subspecies *mexicana*. In addition to these recognizably different clinical forms it is quite possible that the classical Old World type of Oriental sore has been established in Brazil and accounts for some of the cases which do not involve the mucous membranes.

Visceral strains caused by *L. donovani*, produce generalized infections in monkeys, dogs, hamsters, and mice, and sometimes rats, but cats, rabbits, and guinea pigs are relatively insusceptible. Cutaneous inoculations sometimes produce only local skin sores in monkeys and dogs. Cutaneous strains, caused by *L. tropica*, on the other hand, produce only local infections in dogs, cats, monkeys, rats, and guinea pigs, whereas in mice they often produce generalized infections, often with skin lesions as well. The variety *brasilensis* produces visceral infections in hamsters, but produces less severe effects in mice, rats, and cotton rats. Geiman (1940) found that *L. tropica* develops readily in the chorio-allantoic fluid of a 5- to 9-day-old chick embryo, whereas *L. brasilensis* does not, though the original organisms may survive to a second passage.

The difference between visceral and cutaneous infections seems clearly to be one of virulence of the parasites. The body defenses, except in mice, are capable of localizing the cutaneous strains of *Leishmania*, thus confining them to the skin or testicles where inoculated, whereas they are unable to exert a similar restraining action on the visceral strains.

LEISHMANIA DONOVANI AND KALA-AZAR

Kala-azar is a disease that is insidious in origin, slow in development, and fearful in effects. In 1890-1900 an epidemic swept Assam which depopulated whole villages and reduced populations over large areas. In 1917 another epidemic started in Assam and Bengal, reached its height about 1925, and then mysteriously subsided until, by 1931, it was almost gone. In 1937 a new outbreak began in Bihar. In other parts of the world it is less subject to such vacillations. A few decades ago kala-azar brought terror and persecution in its path. Today, knowledge of its epidemiology, diagnosis, and treatment has shorn it of much of its power for evil.

In the Old World typical kala-azar occurs in India, particularly in Assam, Bengal, and Bihar; in North China; in Turkestan; and in Sudan and many other places in tropical Africa; around the Mediterranean and in western and middle Asia; and from Venezuela to northern Argentina in South America.

In kala-azar the parasites are widely distributed in the body, but the special habitat seems to be the large endothelial cells of blood vessels and lymphatics. They are especially abundant in the spleen, liver, and bone marrow, but they are by no means confined to these organs. They are found both inside and outside of the tissue cells, and are present in limited numbers in the circulating blood, usually inside of monocytes, but occasionally free.

Kala-azar is a house and site infection, and for this reason it was once thought that the infection spread by contaminated soil. Although now established that sandflies (*Phlebotomus*) (see pp. 647-654) are the principal vectors, the parasites may sometimes be transmitted by nasal secretions, urine, and feces; infection by mouth is possible in experimental animals. Archibald and Mansour (1937) infected monkeys by swabbing or spraying the nose with infected nasal secretion and also by confining them in an insect-proof room with infected comrades. As noted on p. 139, dogs are important reservoirs of the disease in the Mediterranean area and in South America, are susceptible in China, but seem not to be involved very much in India or Sudan. In the Mediterranean area it is probable that transmission from dog to man is more frequent than from man to man. A similar situation exists between cutaneous leishmaniasis of dogs and man. Cats are sometimes infected, and occasionally horses, sheep, and bullocks. Experimentally monkeys, mice, hamsters, and ground squirrels are susceptible.

All the known or suspected transmitters of kala-azar in the Old World (see pp. 652-653) belong to the *P. major* group of *Phlebotomus* flies. These were listed on p. 139. Adler and Theodor suggested that the frequent occurrence of kala-azar in dogs and infants in the Mediterranean region, and not in India or China, may be due to the fact that the Mediterranean vectors may infect their victims very frequently by direct inoculation into the skin at the time of biting, whereas the Indian and Chinese vectors less frequently inoculate the parasites by their bites but cause infection by being crushed. Since dogs and babies are not so adept at slapping the flies as are adults, they escape infection.

Whether any species of *Phlebotomus* in the United States can serve as transmitters is not yet known.

The Disease. In kala-azar the reaction to parasitization of the reticulo-endothelial cells in internal organs leads to a great increase in their number, especially in the spleen and liver, which may become grotesquely enlarged.

The disease often comes on with symptoms suggestive of typhoid, malaria, or dysentery, and may actually be precipitated by these diseases, for there is now evidence that there is a high natural resistance to kala-azar and that probably the parasites are held under control in many latent infections, and no symptoms appear until resistance is lowered. In a case that Adler experimentally infected by inoculation of a massive dose of cultured *Leishmania*, no symptoms appeared over a period of 9 months, although numerous parasites were found post-mortem. The incubation period is usually at least several months.

After onset there is an irregular fever with enlargement of spleen and liver, rheumatic aches, anemia, and a progressive emaciation. The leucocytes are reduced in number, and the skin is often edematous. Untreated cases usually die in a few weeks to several years, usually from some intercurrent disease which the patient cannot fight with his macrophage system converted into a *Leishmania* breeding ground. Often, in patients who have been treated and have recovered from the systemic disease, whitish spots develop in the skin and eventually grow into nodules the size of split peas; they occur mainly on the face and neck. This condition is called post-kala-azar dermal leishmanoid. Apparently the parasites are able to survive in the skin after the viscera have become too "hot" for them. A number of cases of extensive lesions in the mouth have been seen in the Sudan, in which the parasites were found in abundance in the oral lesions, although they could not be found in the enlarged liver and spleen. Such cases probably represent intermediate conditions of parasite virulence and host resistance between typical kala-azar and cutaneous leishmaniasis.

The Mediterranean type of the disease in infants and dogs runs a similar course but may be of shorter duration.

Diagnosis. Though the clinical symptoms are highly suggestive in endemic localities, diagnosis should be confirmed either by finding the parasites or by serological tests. Puncture of liver, spleen, or lymph glands is useful in finding the parasites. Some workers recommend sternal puncture, but Shortt considers this less effective and more unpleasant for the patient. Shortt et al. have been able to find parasites in over 75 per cent of cases by examination of a thick edge left after making a blood smear. Another method is to make a smear from the dermis exposed with as little bleeding as possible. Inoculation of NNN culture medium with spleen juice, blood, or bits of excised dermis is a reliable procedure. Shortt particularly recommends seeding 3 or 4 NNN culture tubes with the top of the sediment obtained by centrifuging 2 to 5 cc. of blood added to four times its volume of citrated saline. The tubes are incubated at 22 to 24°C., and flagellates appear in 7 days or later in 90 per cent of untreated cases.

A number of simple serological tests have been recommended. One of the first was Napier's aldehyde test, in which a drop of strong formalin is added to 1 cc. of serum; in positive cases the serum gels and turns milky white; a mere gel is not diagnostic. Precipitates are also formed with organic antimony compounds, resorcinol, alcohol, peptonate of iron, lactic acid, and even distilled water, under conditions in which they are not formed by normal serum. The multiplication of apparently unrelated serum tests was becoming very confusing until Chorine

(1937) showed that most of them are due to increase in euglobulin and decrease of albumin in kala-azar serum.

Treatment. Before the discovery of the striking effectiveness of antimony compounds for all forms of leishmaniasis, the death rate in kala-azar cases was about 95 per cent; now it is less than 5 per cent. Two groups of compounds are used: trivalent ones such as sodium and potassium antimonyl tartrates and sodium antimonyl gluconate, and pentavalent ones, the most extensively used being Neostibosan, Neostam, Solustibosan, and urea stibamine. Some trivalent compounds, such as Anthiomaline and Fuadin, which are very useful in schistosomiasis and filariasis, are less effective against leishmaniasis. The pentavalent compounds have the advantage of being less toxic, more quickly effective, and most of them injectable intramuscularly as well as intravenously, but they are more expensive.

Mediterranean and Sudanese forms of kala-azar do not respond to antimony treatment as well as the Indian form, but they respond well to one of the aromatic diamidines (see p. 165), Stilbamidine. Unfortunately this drug is quite toxic; it causes more or less alarming symptoms after injection, and sometimes dangerous ones weeks or even months later. Also, unlike the antimony compounds, the diamidines and related drugs do not immediately relieve the symptoms of kala-azar, but do so several weeks later, when both patient and physician are getting discouraged.

The great trouble with treatment is the long time that has been required for complete cures. Of the tartrates at least 25 or 30 doses daily or on alternate days, totaling at least 2500 mg., are needed, and of the pentavalent compounds, about 10 or 12 doses, totaling 2700 to 4000 mg., are required. Kirk and Sati in 1947, however, reported excellent results in Sudan kala-azar cases using sodium antimonyl gluconate in large daily doses for only 4 days, and then 2 to 6 more doses, usually after an interval of 2 weeks. They got immediate clinical response; usually gland and spleen punctures were negative after the first four injections. They claimed toxic effects to be negligible.

Prevention. Protection against kala-azar involves avoidance and control of sandflies, which is discussed on page 654. Infected houses and people should be avoided after dusk, when sandflies are biting, unless repellents are used. Habitations where cases have occurred should be sprayed with DDT. Some control can be obtained locally by the establishment of free clinics and treatment of all cases. In endemic regions where the canine disease occurs, Sergeant et al. recommend destruction of all dogs showing evidence of infection by symptoms or blood tests, and of all stray dogs; control of movement of dogs into

and out of infected areas; and prevention of contacts between children and dogs. Destruction of the majority of dogs in Canea on the island of Crete in 1933 led to a markedly lower incidence of human kala-azar in the following year.

ORIENTAL SORE (OLD WORLD CUTANEOUS LEISHMANIASIS)

One of the commonest sights in many tropical cities, particularly those of the eastern Mediterranean region and southwestern Asia, is the great number of children, usually under three years of age, who



FIG. 31. Oriental sore on arm. (From Army Institute of Pathology, photograph 79107.)

have on the exposed parts of their bodies unsightly ulcerating sores, upon which swarms of flies are constantly feeding. In some cities infection is so common and so inevitable that normal children are expected to have the disease soon after they begin playing outdoors, and visitors seldom escape a sore as a souvenir. Since one attack gives immunity, Oriental sores appearing on an adult person in Baghdad brands him as a new arrival, and the same is true in many other tropical cities. Dogs frequently suffer from cutaneous leishmaniasis also, especially on the nose and ears, and undoubtedly constitute an important reservoir. Many other animals develop local and sometimes visceral lesions when inoculated (see p. 141).

The disease is more or less prevalent from the shores of the Mediterranean to central Asia and the drier parts of central and western India, and also in parts of China and in many parts of Africa. It is possible that true Oriental sore has been introduced into South America also,

but here it is obviously difficult to distinguish it from the native South American infection.

The parasites are found in the dermal tissues of the sores, where greatly increased numbers of large monocytes and other reticulo-endothelial cells are literally packed with them. Torpedo-shaped parasites are more commonly found than in kala-azar.

The Disease. Classical Oriental sore (Fig. 31) begins as a small red papule, like an insect bite, which gradually enlarges to a diameter of an inch or more. The covering epithelium eventually breaks down and granulation tissue is exposed, but no pus is evident unless the sore is secondarily infected by bacteria. In uncomplicated cases the ulcer remains shallow and sharply defined by raised edges. It persists from a few months to a year or more. The incubation period varies from a few days to several months. In an outbreak among fresh troops in Quetta the incubation period was over 3 months in more than half the cases.

There may be one sore or several, sometimes many, probably due to multiple infective bites. Neighboring lymph glands may be invaded and become large and painful, but general invasion of the body does not occur; generalized symptoms and changes in the blood are lacking unless there are secondary infections. The "wet" type of cutaneous leishmaniasis, which is rural with ground squirrels and gerbils as reservoirs, occurs along with typical Oriental sore in Turkestan. Its special characters are listed on p. 140.

Transmission. Although the parasites may occasionally be inoculated into broken skin by contact or by flies that have just fed on other sores, the disease is usually transmitted by *Phlebotomus* flies. The pupiparous fly, *Hippobosca canina* (see p. 688), may act as a mechanical transmitter among dogs.

Either *Phlebotomus papatasi* or *P. sergenti* or both occur in most places where Oriental sore occurs. Both are readily infected after feeding on infective material, are frequently found naturally infected, and produce infection when crushed and rubbed into scarified skin. According to Adler, however, some strains of *L. tropica* seem better adapted to *P. sergenti* and others to *P. papatasi*. In Italy *P. perfiliewi*, although primarily zoophilic, is believed to be a vector, and in Algeria *P. longicuspis*; as noted on p. 140, the rural "wet"-sore disease of central Asia is transmitted by *P. caucasicus*. For further details concerning *Phlebotomus* flies see pp. 647-654.

Treatment and Prevention. If only one or a few sores are present, local treatment is best. Since secondary infections are common, the scabs must be removed and the sores cleaned and antiseptically treated

with powders or ointments. Injections of atebirin or berberine sulfate around the sores is said to have good effects. Multiple or chronic sores are best treated by injections of antimony compounds as for kala-azar, although in such cases intramuscular injections of the milder compound, Fuadin, are satisfactory. Usually, if the sores are protected, they heal in 15 to 30 days. Other local treatments with carbon dioxide snow, x rays, and various antiseptic ointments have favorable influence but are not as effective as the methods mentioned above.

Control probably lies largely in keeping the sores on either man or dog protected so that sandflies or other biting insects cannot get at them. It is not likely that insects can become infected from sucking blood elsewhere, since blood cultures are never positive. Inoculation with cultures into unexposed parts of the body is recommended in endemic areas.

AMERICAN CUTANEOUS AND MUCOCUTANEOUS LEISHMANIASIS

As noted on p. 140, there are several clinically different types of cutaneous leishmaniasis in tropical America, ranging from Yucatan and Campeche in Mexico to northern Argentina. The disease is called chiclero ulcer in Mexico and Guatemala, Bay sore in British Honduras, Bosch yaws, forest yaws, and pian bois in the Guianas, espundia in Brazil and eastern Peru, uta in other parts of Peru, and buba in Paraguay. Shattuck (1936) pointed out that heat and moisture characterize the climate of all the endemic foci, with the possible exception of the mountain valleys in Peru where uta occurs.

It is almost always contracted, as is jungle yellow fever, in virgin forests, usually among men gathering chicle, rubber, or maté, or constructing railways through the forests. It is common among chicle gatherers in low-lying rain forest areas in Yucatan, especially from August to January when the collecting season is at its height. Biagi found 62 per cent of these people positive to the Montenegro skin test for leishmaniasis. Although usually acquired in rain forests, outbreaks of leishmaniasis have occurred in residential parts of Rio de Janeiro, where there were gardens and shrubbery, and in Peruvian villages at elevations of 4500 to 7500 feet, where the mild form of the disease known as uta occurs.

Dogs are sometimes found naturally infected, but not as commonly as with Oriental sore in the Old World. Monkeys and dogs can be experimentally infected, and Fuller and Geiman in 1942 found that squirrels, especially Texas ground squirrels, are susceptible to cutaneous but not to intraperitoneal inoculation, and develop ulcerating sores. Hamsters are less easily infected but may develop nodular skin lesions

that do not ulcerate, and also visceral infections. Milder infections can be induced in mice.

Mucocutaneous Leishmaniasis (Espundia). This severe form of the disease occurs from Brazil to Paraguay and northern Argentina. In typical cases the infection begins precisely as in Oriental sore and frequently follows a similar course, but there is a greater tendency for the sores to spread over extensive areas and for more numerous sores



FIG. 32. American leishmaniasis. *A*, a case of the mucocutaneous form from Brazil. (Photograph supplied by Dr. Nery-Guimaraes.) *B*, chiclero ulcer of the ear; a case of moderate duration as commonly seen in southern Mexico. (Photograph supplied by Dr. F. Biagi.)

to appear. In one instance 248 sores were reported. The ears, face, forearms, and lower legs are the favorite sites for the original lesions, but laborers naked to the waist may get ulcers on the trunk, and occasionally on the genitals or elsewhere. Sometimes the sores show a mass of raw granular tissue raised above the surface; at other times they become extensively eroded, with sharply defined, raised, purplish edges and a surrounding red inflamed area. The foul-smelling fluid which exudes sometimes crusts over, but may be inoculated into abrasions elsewhere and cause secondary ulcers. Secondary infections with bacteria, spirochetes, fungi, or maggots are frequent. The rarity of leishmaniasis in late stages suggests that secondary infections may play an important role, though the prompt healing which follows antimony treatment shows that leishmaniasis still play a leading part. There is

nothing about the sores to distinguish them with certainty from others caused by blastomycosis, syphilis, tropical ulcers, or even in some cases yaws, so it is little wonder that there has been much confusion about their distribution and etiology.

The most striking feature of the disease is the secondary development, sometimes by extension but more frequently by metastasis, of ulcerations in the nasal cavities, mouth, and pharynx, which may occur in 20 per cent or more of the cases, though much more commonly in some geographic regions than in others. In rare cases ulcers occur in the vagina. According to Villela et al., small incipient lesions can be found in the nose in many cases in which no obvious lesions are present, and scrapings of the mucosa frequently reveal *Leishmania* even when it is perfectly normal in appearance. The mucous membrane ulcerations may appear before the skin lesions have healed, but usually they develop from several months to several years later. Ordinarily they commence as tiny itching spots or swellings of the mucous membrane, usually in the nose, the infected membrane becoming inflamed, and marked either with small granular sores or with blister-like swellings. The lymph glands in the infected regions become swollen and turgid. A granular ulceration begins in a short time, invading all the mucous membranes of the nose and spreading by means of infective fluid which flows down over the upper lip into the mouth cavity, attacking the hard and soft palate.

Advance of the lesion is obstinate and slow, and gives rise to serious complications. The nostrils become too clogged to admit the passage of sufficient air and the patient has to keep his mouth constantly open to breathe. His repulsive appearance and fetid breath help to make his life miserable. Affections of the organs of smell and hearing, and even sight, may supervene, and the voice is weakened or even temporarily lost. The digestive tract becomes upset from the constant swallowing of the exudations mixed with saliva or food. A spreading of the nose due to the eating away of the septum is a characteristic feature. Although in late stages of the disease the entire surface of the palate and nasal cavities is attacked and the septum between the nostrils destroyed, the bones are left intact, a feature which readily distinguishes a leishmanian ulcer from a syphilitic one. Usually the victim of espundia, if untreated, dies of some intercurrent infection, but he may suffer for years and eventually succumb to the disease itself.

Diagnosis is usually made by finding the leishmanias in the lesions, but a skin test described by Montenegro in 1926 is sometimes helpful. Dead cultured flagellates are injected into the skin; in positive cases an allergic inflammation develops within 48 hours.

Transmission. Little is definitely known about the transmission of the disease, though by analogy with other forms of leishmaniasis it is highly probable that bites of *Phlebotomus* flies are usually responsible. Support for this view is provided by instances in which typical sores developed at the site of bites of *P. lutzi* in Brazil. Aragão in 1922 found leptomnads in some wild *P. intermedius* captured in a locality in Rio de Janeiro where a local outbreak occurred, and in five of the flies that had fed on espundia sores 3 days before, he found similar flagellates. When emulsions of these flies were inoculated into the nose of a dog, an ulcerating sore containing leishmanias developed 3 days later. Natural or experimental infections of this species, a semidomestic one, have been reported in many South American countries, from Argentina to Venezuela. Natural and experimental infections have been reported in at least six other species in various parts of South America (Bustamente, 1948). For further details see pp. 647-654. In Peru Townsend obtained some experimental evidence that two species of midges of the genus *Forcipomyia* (see p. 657) are the transmitters of uta, but this work needs confirmation.

Treatment. Most cases respond well to injections of antimony compounds, but some respond better to Neosalvarsan, and in some cases resistant to antimony and arsenic compounds, Lomidine, one of the diamidines (see p. 165), has proved effective. Treatment should be accompanied by removal of scabs from ulcers, even on nose, lips, or mouth, and cleansing to get rid of bacterial infections. In lesions confined to the skin local treatments are helpful, using antimony tartrate applied as a powder or in 1 or 2 per cent solutions, or the methods described for Oriental sore can be employed. For chiclero ulcers the local treatments are satisfactory except for the chronic ear lesions, which requires systemic treatment with tartar emetic, Fuadin, or Lomidine.

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• 8 •

Hemoflagellates

II. Trypanosomes

One of the blackest clouds overhanging the civilization of tropical Africa is the scourge of trypanosome diseases which affect both man and domestic animals. The ravages of sleeping sickness, which is the final phase of trypanosome infection in man, were well known to the old slave traders, and the presence of "lazy niggers" lying prostrate on wharves and docks with saliva drooling from their mouths, insensible to emotions or pain, was a familiar sight. It did not take these astute merchants long to find that death was a frequent outcome of the disease, and they soon recognized swollen glands in the neck as an early symptom and refused to accept as slaves Negroes with swollen glands. Nevertheless sleeping sickness must often have been introduced with its parasites into various parts of North and South America, as it frequently is even at the present time, and only the absence of a suitable means of transmission has saved the western hemisphere from being swept by it.

In Africa the most obvious effect of sleeping sickness is depopulation by death, induced sterility, high infant mortality, and displacement of population, with the result that the land is relinquished to wild animals and tsetse flies. Important as human infection has been in Africa, the effect of trypanosomiasis on domestic animals has, over vast areas, had a tremendous influence on the economy and development of that continent. As Hornby (1949) remarked, "Trypanosomiasis is unique among diseases in that it is the only one which by itself has denied vast areas of land to all domestic animals other than poultry. The areas of complete denial are all in Africa and add up to perhaps one quarter of the total land surface of this continent." Animal trypanosomiasis, by making it impossible to keep cattle or other animals, causes loss of soil fertility by the absence of manure, diminishes vitality of the people because of deficiencies in the diet, and deprives them of beasts of burden.

Fossil remains of tsetse flies, belonging to the Oligocene period, have been found in Colorado, and it has been suggested that the extinction

of prehistoric camels and horses in North America, which cradled them in the early days of their evolution, may have been brought about by tsetse-borne trypanosome diseases.

History. Although trypanosomes were first discovered in 1841, which is very ancient history in parasitology, the first connection with disease was the discovery in 1880 that they were the cause of surra in horses and other animals in India. In 1895 Bruce showed that nagana of domestic animals in Africa was caused by trypanosomes. In 1902 Forde and Dutton discovered the presence of trypanosomes in human blood in a case of "Gambia fever," the preliminary stage of sleeping sickness. In 1903 Castellani found trypanosomes in the cerebrospinal fluid of cases of sleeping sickness in Uganda. Kleine, in 1909, showed that the tsetse fly is no mere mechanical transmitter but a true intermediate host. In that same year there was discovered a new type of human sleeping sickness in Rhodesia, and Chagas described an entirely different human trypanosome infection in South America.

The Parasites. The general relationships of trypanosomes have been discussed on pp. 134-135. They may be regarded as having developed in the course of evolution from the crithidias of invertebrates, adapted to living in the blood of vertebrates on which the invertebrates habitually feed. They thus bear the same relation to *Crithidia* that *Leishmania* bears to *Leptomonas*.

Trypanosomes exist as parasites in all sorts of vertebrates—fish, amphibians, reptiles, birds, and mammals—living in the blood, lymph, or tissues of their hosts. A great number of different species have been named; usually any trypanosome found in a new host is named after the host as a tentative label until more is found out about it. Though this procedure is not in accordance with rules of naming animals, it is better than the alternatives of having numerous nameless trypanosomes to deal with, or of identifying them with species from which they may subsequently be found to differ.

In form most trypanosomes are active, wriggling little creatures somewhat suggesting diminutive dolphins or eels, according to their slenderness (Fig. 33). They swim in the direction of the pointed end of the body, being propelled by the wave motions of the undulating membrane. The body is shaped like a curved, flattened blade, tapering to a fine point anteriorly, from which a free flagellum often continues forward. This flagellum continues nearly to the posterior end of the body, and is connected with the body by an undulating membrane, like a long fin or crest; in some species it is thrown into numerous graceful ripples; in certain others, e.g., *Trypanosoma cruzi*, it is only slightly rippled. The body contains a nucleus which varies in its posi-

tion in different species and under different circumstances. Near the posterior end, or sometimes at the tip, there is a kinetoplast and a basal granule from which the flagellum arises. The kinetoplast is lost in *T. equinum* and some strains of *T. evansi*, species which have become independent of intermediate hosts; apparently, as Hoare has pointed out, the kinetoplast is necessary for development in tsetse flies, but not for multiplication in vertebrate hosts. Many species also contain scattered, deep-staining granules in the cytoplasm. Trypanosomes are

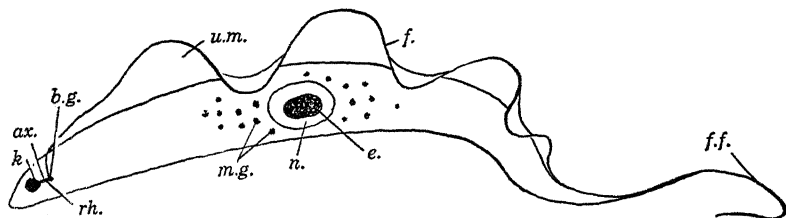


FIG. 33. *Trypanosoma gambiense*, slender form; ax., axoneme; f., flagellum; f.f., free flagellum; k., kinetoplast; m.g., metachromatic granules; n., nucleus; rh., rhizoplast; u.m., undulating membrane.

commonly spoken of as polymorphic or monomorphic. Polymorphic forms are those in which some individuals have a free flagellum and others do not, e.g., *T. gambiense*, *brucei*, and *rhodesiense*, whereas monomorphic forms may always have a free flagellum, e.g., *lewisi*, *cruzi*, *vivax*, *evansi*, *equinum*, and *equiperdum*, or may always lack one, e.g., *congolense*, *simiae*.

Life Cycles. In the vertebrate hosts most trypanosomes usually multiply by simple fission. The kinetoplast is the first structure to divide; next a new flagellum begins to grow out along the margin of the undulating membrane; then the nucleus divides; and finally the body splits from the anterior end backwards.

The African polymorphic trypanosomes of man and animals are mainly parasites of the lymphatic and intercellular fluids, but multiplication also occurs in the blood stream; *T. equiperdum* thrives in edematous fluid of sex organs and skin; and some trypanosomes of birds apparently live mainly in the bone marrow. *T. cruzi*, however, multiplies intracellularly in a leishmania form (Fig. 39), changing to the trypanosome form before being liberated from the cells; the free trypanosome forms get into the lymph and blood but do not multiply there (see p. 167). Because of these peculiarities some workers, notably Dias, prefer to place this species in a separate genus, *Schizotrypanum*, intermediate between *Leishmania* and *Trypanosoma*. In many cases the favorite habitat of trypanosomes is unknown, only the blood

forms having been recognized. In some species at least, e.g., *T. lewisi* of rats and *duttoni* of mice, an immune response which inhibits reproduction soon develops, making further multiplication impossible.

At least one trypanosome, *T. equiperdum*, has become completely independent of its ancestral invertebrate hosts and is transmitted directly from horse to horse during copulation, and other trypanosomes can live and multiply indefinitely in vertebrate hosts if artificially injected by the soiled proboscis of biting flies. The majority of them, however, when they reach a suitable invertebrate host, hark back to the traditions of their remote forebears and go through a cycle of development more or less like that of typical crithidias. Some, such as *T. cruzi* and *T. lewisi*, finding themselves in the ancestral home, revert almost completely. After being sucked into the stomach of an insect they assume the crithidial form, attach themselves to the epithelial cells or enter them, and multiply. Gradually they move backwards towards the rectum, and the infective forms are voided with the feces. Infection occurs either by contamination of the bite with the feces, which is probably the usual way in *T. cruzi*; by ingestion of the feces of the insect when licking the bites, as in the case of *T. lewisi*; or by ingestion of the whole insect.

Those trypanosomes which develop thus in the hindgut of invertebrates are said to develop in the posterior station; they are the conservatives. The trypanosomes of this group use a variety of invertebrates as intermediate hosts; for example, *T. lewisi* of rats develops in fleas, *T. melophagium* of sheep in sheep ticks (keds), *T. theileri* of cattle in tabanids, *T. cruzi* of man and other animals in triatomid bugs, and African reptilian trypanosomes in tsetse flies. There are other trypanosomes, however—the radicals—which after ingestion by their insect vectors develop in the anterior part of the alimentary canal and infect by way of the proboscis. They form an evolutionary series: first the *T. vivax* group, which develop only in the proboscis; then the *congolense* group, which develop first in the stomach and then move forward to the pharynx; and finally the *brucei* group, which, after some development in the stomach, move forward and invade the salivary glands, where the cycle of development is completed. So far as known at present, this specialized procedure occurs only in tsetse flies, which serve as transmitters of African mammalian trypanosomes, and in leeches, which transmit the trypanosomes of aquatic animals. Such trypanosomes are said to develop in the anterior station. The infective trypanosomes that appear at the end of the cycle in insects, whether in the anterior or posterior station, are called metacyclic forms; they resemble the blood forms but are smaller.

Identification of Mammalian Trypanosomes. The following key indicates the principal differences between some of the commoner mammalian trypanosomes:

- I. Polymorphic forms; undulating membrane convoluted; kinetoplast usually not terminal; body with metachromatic granules. Invade salivary glands of tsetse flies.
 1. Nucleus nearly always central or slightly posterior; low virulence for domestic and laboratory animals (Fig. 34, 1 and 2).....*T. gambiense*.
 2. Nucleus sometimes posterior, especially in small laboratory animals (Fig. 34, 3); highly virulent in laboratory and domestic animals.
 - a. Man not susceptible.....*T. brucei*.
 - b. Man infectible.....*T. rhodesiense*.
- II. Monomorphic forms with free flagellum.
 1. Undulating membrane only slightly convoluted.
 - a. Kinetoplast small, not terminal; nucleus anterior; length about 25 μ ; parasite of rats; develops in fleas (Fig. 34, 6).....*T. lewisi*.
 - b. Kinetoplast large, egg-shaped, usually terminal; nucleus central; body stumpy; length about 20 μ ; parasite of various small mammals and man; develops in triatomids (Fig. 34, 5).....*T. cruzi*.
 2. Undulating membrane moderately or strongly convoluted.
 - a. Size large, usually 50–70 μ long; kinetoplast distant from posterior end.
 - (1) In cattle; develops in tabanids (Fig. 34, 7).....*T. theileri*.
 - (2) In sheep; develops in sheep-tick.....*T. melophagium*.
 - b. Size moderate (18–36 μ).
 - (1) Posterior end swollen and rounded; undulating membrane moderately convoluted; kinetoplast terminal or nearly so; highly pathogenic for domestic animals, but laboratory animals insusceptible; develops in tsetse fly in proboscis only (Fig. 34, 10).....*T. vivax*.
 - (2) Posterior end pointed.
 - (a) Nucleus consistently anterior (three-eighths length of body from anterior end); kinetoplast small, subterminal; extremely long and slender forms develop in cultures; develops in *Rhodnius* (Fig. 42).....*T. rangeli*.
 - (b) Nucleus central or slightly posterior; kinetoplast small, subterminal; undulating membrane well convoluted, closely resemble flagellated phase of *brucei* (Figs. 33, 34, 1).
 - (1) Highly pathogenic for horses, dogs and camels, causing surra, milder in cattle; transmitted by biting flies mechanically.....*T. evansi*.
 - (2) Milder in dogs, causes dourine in horses; venereally transmitted, with no insect intermediary. *T. equiperdum*.
 - (c) Similar to (b) but kinetoplast absent; causes mal-de-caderas in horses in South America (Fig. 34, 4).....*T. equinum*.
 - III. Monomorphic forms with no free flagellum.
 1. Small, 9–18 μ long; kinetoplast terminal or nearly so; produces chronic wasting disease in domestic animals, especially destructive to cattle; not highly virulent for laboratory animals; develops in stomach and pharynx of tsetses, not in salivary glands (Fig. 34, 8).....*T. congolense*.

2. Larger, 14–24 μ long; highly virulent for pigs; monkeys, sheep, and goats also susceptible, but usually not other domestic or laboratory animals (Fig. 34, 9) *T. simiae*.

Pathogenicity and Immunity. The very name trypanosome suggests deadly disease, yet at least the majority of trypanosomes are harmless to their hosts. Wenyon in 1926 went so far as to say: "As a general statement, it is safe to regard all trypanosomes as nonpathogenic to their natural hosts." The so-called pathogenic trypanosomes

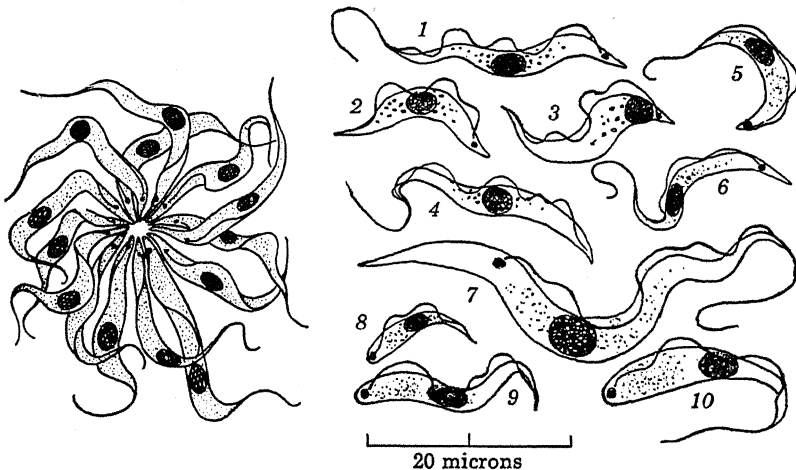


FIG. 34. Left, agglomeration of trypanosomes, *T. lewisi*, in blood of immunized rat. (After Laveran and Mesnil.) Right, mammalian trypanosomes: 1, *brucei* or *gambiense* with free flagellum; 2, same, without free flagellum; 3, *brucei* or *rhodesiense*, form with posterior nucleus; 4, *equinum*; 5, *cruzi*; 6, *lewisi*; 7, *theileri*; 8, *congolense*; 9, *simiae*; 10, *vivax*.

of man and domestic animals he regards as owing their injuriousness to their being in unnatural hosts; in the wild game animals of Africa, which he regards as the natural hosts, they are harbored without ill effects. *T. gambiense* has undoubtedly arisen from a *brucei*-like ancestor; it has not yet reached a stage of equilibrium with its new host where it can exist without creating a disturbance. It is significant that where human infections have existed longest the disease tends to assume a mild chronic form. *T. rhodesiense*, a more recent offshoot from *T. brucei*, is much more pathogenic for man.

The pathogenicity of trypanosomes depends largely on ability of the hosts to develop trypanocidal antibodies and in some cases reproduction-inhibiting antibodies (Taliaferro, 1926). Vitamin deficiencies may increase their harmfulness; Becker et al. in 1947 showed that the

usually benign *T. lewisi* may become pathogenic in pantothenate-deficient rats. The serum of a recovered animal contains protective antibodies against the particular trypanosome involved, and shows the usual immune reactions, such as complement fixation and lysis. It also causes the trypanosomes to clump together in rosettes, attached by their posterior ends (Fig. 34, left), and to adhere to leucocytes and platelets in the blood. Serum of naturally immune animals protects against infection when injected but is not destructive *in vitro*.

African Trypanosomiasis and Sleeping Sickness

Two distinct types of trypanosomes cause human disease, one type in Africa, the other in South and Central America. The African trypanosomes belong to a group of closely related polymorphic forms. One of these, *Trypanosoma brucei*, is found in many African wild animals, is highly virulent for domestic animals, especially horses and camels, is infective for almost every kind of mammal except baboons and man, and is transmitted by *Glossina morsitans*. This is without doubt the parent form from which two species or strains capable of infecting man have arisen, namely, *T. gambiense* and *T. rhodesiense*. Some authorities consider both of them distinct species, some think that *gambiense* but not *rhodesiense* is distinct from *brucei*, and some think that all of them are mere strains of a single species.

It seems evident that here again, as in the case of spirochetes, amebas, and leishmanias, we have run up against the difficulty in classification that comes from the fact that pathogenic organisms are not immutable things that can be described like simple chemical compounds, but are constantly undergoing adaptation and change. Their evolutionary possibilities are great because of their rapid multiplication, and are further enhanced by the isolation and variety of environmental conditions afforded them by life in a variety of intermediate and definitive hosts.

Aside from minor and inconstant differences in behavior in tsetse flies and in effects on laboratory animals, the only difference between *T. gambiense* and *T. rhodesiense* is the fact that the latter, like *T. brucei*, when developing in small laboratory animals produces a small percentage of forms in which the nucleus is displaced to the posterior end of the body. Even this is not a constant difference, and it is possible that it results from unusually rapid multiplication, and may be only an indication of virulence of the parasite or susceptibility of the host.

Morphology and Habits. The African polymorphic trypanosomes vary in length from about 15 to 30 μ , with exceptionally longer or

shorter forms. They show the characteristic slender forms with free flagellum, stumpy forms without a free flagellum, and intermediate forms, in any single blood or gland smear (Fig. 35). They are nearly always sparse in human blood, and are usually more abundant in the juice of enlarged lymph glands. They also occur in the spleen, which is often enlarged. Later, usually after 3 months, they appear in the cerebrospinal fluid and even in the tissues of the brain and spinal cord.

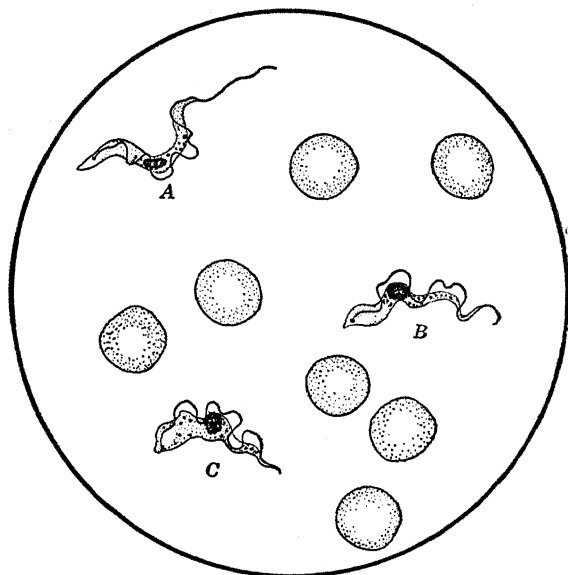


FIG. 35. *Trypanosoma gambiense* showing A, long form with free flagellum; B, intermediate form; and C, short form without free flagellum. About $\times 1200$.

Throughout the infection they live between the cells and are only found inside the cells when they have been ingested by phagocytes. These trypanosomes in the past have not been easily cultured in artificial media, but Weinman has succeeded with a medium containing blood, peptone, and beef-heart infusion. The cultured forms resemble those that develop in tsetse flies; they are not infectious but they are antigenic. The trypanosomes can also be cultured in chick embryos.

Trypanosoma gambiense is readily inoculated into certain kinds of monkeys and less readily into small laboratory animals, unless first passed through a monkey. Various antelopes and other herbivorous animals, and also dogs, are susceptible. The Situtunga antelope is an important natural reservoir in some places, and domestic animals, particularly pigs, may also serve in this capacity.

T. rhodesiense parasitizes wild game and domestic animals as well as man. Normal human serum is toxic to all the African trypanosomes except *T. gambiense* and *T. rhodesiense*, but whereas *T. gambiense* apparently never loses this immunity, *T. rhodesiense* may do so after being kept in culture or in laboratory animals for a long time. This suggests that *T. rhodesiense* is a strain that has not become as thoroughly acclimated to human blood as *T. gambiense*, which is also indicated by its greater virulence.

Distribution. Human infections with *Trypanosoma gambiense* occur in a wide area in tropical western Africa from Senegal to Loanda, extending inland along the rivers, particularly the Congo and Niger. The affected areas have been extended to Lake Tanganyika and southern Sudan by white settlement and consequent movement of infected natives. Stanley's expedition to reach Emir Pasha in 1888 may have introduced the disease to virgin territory in Uganda and the Great Lakes region, where it gave rise to a terrible epidemic that in one district reduced the population from 300,000 in 1901 to 100,000 in 1908. Some whole villages and islands were depopulated. Buxton (1948), however, suggested that this outbreak may have been due in part to *T. rhodesiense*, which was unknown at that time.

In more recent years the severity of the disease has been reduced in many parts of Africa by preventive measures and treatment, together with a natural decrease in virulence in many areas. In Nigeria alone, from 1931 to 1943, over 4,000,000 examinations were made, with detection and treatment of over 300,000 cases. The infection rate in Nigeria is now only one-tenth of what it used to be. However, in many endemic areas in Africa, 5 to 30 per cent or more of the natives are still infected.

T. rhodesiense infection was first reported in Rhodesia in 1909. Since then many more cases have occurred over a fairly wide area in eastern Africa from Kenya to southern Rhodesia and northern Mozambique, and inland across Tanganyika to Uganda and eastern Congo. A few outbreaks that might be termed epidemics have occurred, including one in Uganda in 1940-1943, but in general the infection in *T. rhodesiense* areas is markedly sporadic. This species has a tendency to recur in certain spots, sometimes after intervals of many years. In spite of its greater pathogenicity and high case mortality rate, it affects such a small percentage of the population as to be a relatively minor public health problem. Animal trypanosomiasis has far more serious effects on the welfare of East Africa.

Transmission and Epidemiology. The entire group of polymorphic trypanosomes is transmitted by tsetse flies; they differ from

other tsetse fly-transmitted trypanosomes by invading the salivary glands of the flies. Although animal trypanosomiasis is often transmitted mechanically by biting flies, such as tabanids and *Stomoxys*, this method of transmission is negligible as far as man is concerned, although mechanical transmission by tsetse flies may not be infrequent.

The species of tsetse flies involved vary with the strains. The principal vector of *brucei* and *rhodesiense* is *Glossina morsitans*, although in one part of Tanganyika *G. swynnertoni* is also an important carrier. In the Uganda epidemic of *T. rhodesiense* in 1940–1943, *G. pallidipes*

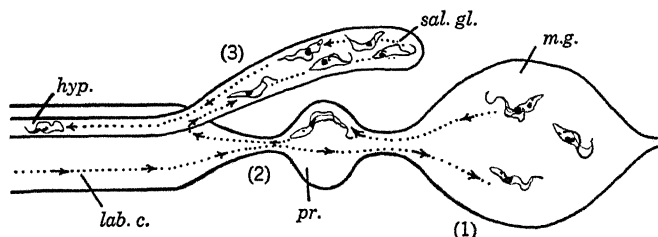


FIG. 36. Course of development of *T. gambiense* in tsetse fly. (1) multiplication in midgut in trypanosome form; (2), long, slender trypanosomes in proventriculus; (3) passage to salivary glands and development there of crithidial and then infective trypanosome forms; hypopharynx and labial cavity used for passage only; *hyp.*, hypopharynx; *lab.c.*, labial cavity; *m.g.*, midgut; *pr.*, proventriculus; *sal.gl.*, salivary gland.

seemed to be the principal transmitter. The principal vector of *gambiense* is *G. palpalis*, but in northern Nigeria and Cameroons *G. tachinoides* seems to be the important transmitter. These species of *Glossina* are discussed on pp. 681–682. Experimentally *T. brucei* and *rhodesiense* can also be transmitted by *G. palpalis* and other tsetses, and *T. gambiense* by *G. morsitans*.

When cyclical development occurs (Figs. 36 and 37), the ingested parasites multiply first in the middle intestine. After the tenth to fifteenth day long slender forms are developed which move forward to the proventriculus. After several more days the trypanosomes make their way to the fly's salivary glands, to the walls of which they attach themselves by their flagella and, rapidly multiplying, undergo a crithidial stage. As multiplication continues, free-swimming "metacyclic" trypanosome forms are produced which very closely resemble the parasites in vertebrate blood and are now capable of infecting a vertebrate host. The whole cycle in the fly usually occupies 20 to 30 days. A temperature between 75°F. and 85°F. is necessary for the full development of the parasite in the fly, ending in invasion of the salivary glands.

In nature not more than 1 or 2 per 1000 wild tsetses are found

infected with trypanosomes of the *brucei* group although 20 to 30 per cent of the game on which they feed are infected. Many flies appear to be completely refractory to infection, as Huff has shown to be true of mosquitoes and malaria. On the other hand, individuals gifted with susceptibility are often found to be infected with more than one

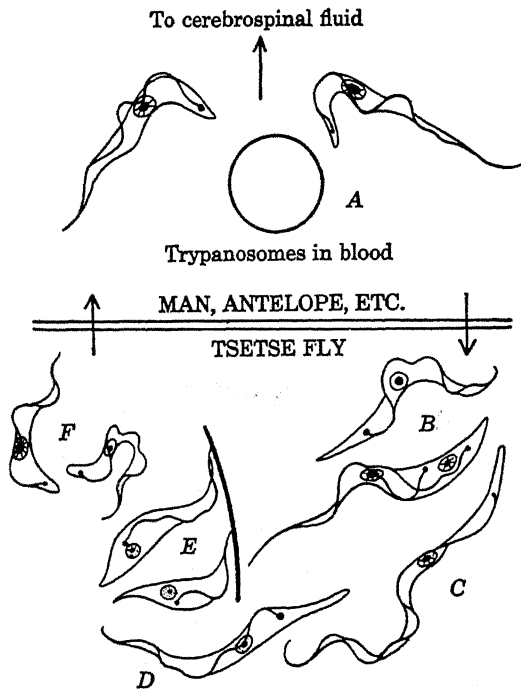


FIG. 37. Life cycle of *T. gambiense*. *A*, long and short forms in human blood; *B*, trypanosomes in midgut of tsetse 48 hours after blood meal; *C*, slender proventricular forms, 10th to 15th day; *D*, trypanosome newly arrived in salivary glands, 12th to 20th day; *E*, crithidias in salivary glands, 15th to 25th day; *F*, infective trypanosomes in salivary glands, 20th to 30th day. (Constructed from figures by Robertson, *Proc. Roy. Soc. London*, 1912.)

species of trypanosome. Strains of trypanosomes vary in their ability to infect the salivary glands of tsetses, and some lose their power of cyclical transmission entirely after prolonged cultivation or passage through animals.

As noted above, game animals may serve as reservoirs for the human trypanosomes, particularly *T. rhodesiense*. The recurrence of *rhodesiense* infections in the same spots raises the question whether man or some animal is the more important reservoir (Buxton, 1948). Healthy human carriers exist and might be responsible for keeping the

disease alive, but it is also known that this trypanosome remains capable of infecting man even after a long succession of cyclically transmitted passages to sheep or antelopes, although virulence for man then diminishes. The *rhodesiense* infection usually occurs on the fringes of thinly populated back country abounding in big game, whereas *gambiense* infections prevail in well-populated areas with sparse mammalian fauna. It is reasonable to believe that man-to-man transmission is the usual thing in *gambiense* infections, but that animal-to-man transmission plays an important part in *rhodesiense* infections. Outbreaks of *gambiense* infections tend to be widespread and prolonged, whereas *rhodesiense* outbreaks are limited and brief. In part, at least, this is because natives infected with *rhodesiense*, by the time the trypanosomes appear in their blood, are far too ill to venture into the "bush" where *Glossina morsitans* could suck up their parasites, whereas the mild, prolonged course of the *gambiense* disease enables infected people to carry on with their usual occupations for months or years, and to serve as sources of infection for tsetses.

The habits and characteristics of the vectors of the two infections also contribute. The *gambiense* vectors and man both require water; therefore in dry seasons in poorly watered areas the concentration of flies and man in limited areas provides ideal conditions for the spread of a parasite that does not easily infect tsetses and is not easily transmitted by them. The people spread the infection along trade routes, by local travel, or by movement away from a decimated locality. This, according to Morris (1951), accounts for the great epidemics in the interior savanna woodlands of West Africa and their absence in the wetter forested coastal areas, where the flies, though abundant, are free to wander, and may only occasionally bite another person after picking up an infection. In East Africa the vectors of *rhodesiense* infections are not so dependent on water, and concentrations of man and flies in the same place is of less frequent occurrence, hence the lesser frequency and more limited nature of the outbreaks.

The Disease. The course of the disease caused by trypanosome infection is insidious and irregular. The Gambian and Rhodesian diseases are essentially alike in their symptoms and in the course they run, except that the latter is usually more rapid in development and more virulent in effect, as a rule causing death within 3 or 4 months after infection, often without the enlarged glands so characteristic of *gambiense* infections. The variety of the Gambian disease found in Nigeria is comparatively mild and of long duration.

The bite of an infected tsetse fly is usually followed by itching and irritation near the wound, and frequently a local, dark-red, button-like

lesion develops, occasionally increasing to considerable size. After a few days, fever and headache develop, recurring at irregular intervals for weeks or even months, accompanied by increasing weakness, enlarged glands, and usually some edema, and a markedly lowered resistance to other diseases. Often a peculiar tenderness of the muscles is complained of also. Usually an irritating rash breaks out during the early stages of the disease. Sometimes for long intervals trypanosomes are so sparse in the blood that they can be detected only by animal inoculation. Loss of ambition and vitality usually figure prominently, and childbirth is seriously interfered with.

It is possible that after weeks or months or years of irregular fever and debility the disease may spontaneously disappear and never become more than trypanosome fever. Usually, however, the parasites ultimately succeed in penetrating to the cerebrospinal fluid of the brain and spinal cord, and "sleeping sickness" results.* In the Rhodesian disease the central nervous system is usually invaded early, but in the Gambian disease this is a late manifestation and may appear from a few months to at least 7 years after the onset of symptoms. The invasion is accompanied by a striking accumulation of round cells in and around the walls of vessels in the brain and by characteristic increases in the cells of the cerebrospinal fluid.

Sleeping sickness is ushered in by an increase in the general physical and mental depression. The victim wants to sleep constantly and lies in a stupor; his mind works very slowly, and even the slightest physical exertion is obnoxious. Eventually the sleepiness gets such a hold on him that he is likely to lose consciousness at any time and even neglects to swallow his food. After weeks of this increasing drowsiness his body becomes emaciated, a trembling of the hands and other parts of the body develops, with occasional muscular convulsions and sometimes maniacal attacks. He finally passes into a state of total coma ending in death, or death may end the unhappy condition earlier during an unusually intense convulsion or fever, or through the agency of some complicating disease. If untreated, death is probably the inevitable outcome. A large percentage of infections occurs among people of middle age; old people are significantly few in number in sleeping sickness districts.

Diagnosis. Diagnosis should be confirmed by finding the parasites in blood or gland juice in early cases, or in cerebrospinal fluid when symptoms or increased cells suggest involvement of the central nervous system. Often the parasites are very scanty, and inoculation of lab-

* It should be noted that the so-called sleeping sickness of the United States is a totally different disease, caused by a filtrable virus.

oratory animals may have to be resorted to. Blood can be examined by centrifuging it twice, just enough to throw down the red cells each time, removing the supernatant and leucocyte cream, and recentrifuging this at high speed for a long time, then examining the sediment. Sometimes the parasites are detectable by their movement in fresh, fairly thick preparations, or they may be found in Giemsa-stained thick smears.

Examination of gland juice obtained by puncturing an enlarged gland with a dry needle is usually more reliable in early cases, and in late cases centrifuged cerebrospinal fluid is more frequently positive than is the blood. Marrow obtained by sternal puncture is sometimes positive, but less often than in leishmaniasis.

Treatment. Arsenic and antimony compounds were until recently the standard drugs for treatment of trypanosomiasis, but now they are rarely used except for late stages when the parasites have invaded the central nervous system. Two drugs, Bayer 205 (also called Antrypol, Germanin, or Suramin), and pentamidine or a closely related drug, Lomidine, which are aromatic diamidines, are now most widely used for both treatment and prophylaxis of human infections; they are low in toxicity, effective in treatment, and prevent reinfection for several months.

For treatment of blood and lymph infections, five intramuscular injections of pentamidine or Lomidine at 2-day intervals, at the rate of 4 mg. of the base per kilogram of weight, have been found to produce no damage to the nervous system, liver or kidneys, and to be followed by very few relapses, in over 12,000 cases in French West Africa (Jonchére, 1951), although the immediate transient reactions characteristic of the diamidines were observed. Antrypol has a buffer effect on the diamidines, preventing their toxic effects, so a combination of the two drugs may permit larger doses and effective treatment in 2 or 3 days, possibly in 1 day. Lourie (1953) thinks that a combination of these two drugs might be particularly advantageous in mass prophylaxis (see below). This case of two drugs, apparently acting together therapeutically, but one annulling the other's toxic effects, seems to be unique in therapeutics.

The prophylactic effect of Antrypol is due to the fact that this combines with globulin in the blood and remains in the circulation. Presumably the long-lasting effects of the diamidines and also Antrycide (see p. 177) may be similarly explained. Single injections of pentamidine or Lomidine, or two injections of Antrypol (0.5 gram followed by 1.5 grams after 2 days), prevent reinfection for about 6 months or more. In French West Africa and Belgian Congo, where prophylactic

doses have been given to hundreds of thousands of people, infection rates have been reduced in the treated people by 90 to 99 per cent after 3 to 5 treatments at 6-month intervals, and even in untreated people there has been 50 to 65 per cent reduction.

After invasion of the central nervous system, an arsenic drug, Tryparsamide, is the only effective drug known that is reasonably safe, but even it is very toxic, and strains of trypanosomes resistant to it have cropped up all over Africa. Tryparsamide treatment requires a series of once-a-week injections of 0.04 gram per kilo for 10 or 12 weeks, usually repeated once or even twice after 3-month intervals, so that a completed treatment takes as long as a year. The drug sometimes injures the optic nerve and may cause blindness.

As an alternative for cases that do not respond to Tryparsamide, melarsen oxide, a trivalent arsenic compound, was suggested by Weinman in 1946, and a supposedly detoxified derivation of it, Mel B, by Friedheim in 1949. Jonchère et al. (1953) think that both drugs, although very effective in treatment, are so toxic and have such a narrow margin of safety that they should be used only in cases which have failed to respond to Tryparsamide and are sure to die if left untreated. Thus far no method of dealing with drug-fast strains of trypanosomes has been found except the use of a variety of different drugs, for the parasites obstinately retain their resistance even after passage through tsetse flies.

Prevention. Therapeutic and prophylactic treatment, including the establishment of sleeping sickness dispensaries, can certainly reduce human infection to a low level, and possibly locally eradicate it in the case of *gambiense* infections. It is more difficult in *rhodesiense* areas because the disease is more rapidly fatal, and wild animals play a much larger role in its epidemiology. Aside from mass treatment and prophylaxis, control of human trypanosomiasis resolves itself into getting rid of tsetse flies, or reducing contacts between them and the human population, by one or more of the methods discussed on pp. 683-684. Wholesale evacuation of human inhabitants of an area, as was done in the great Uganda epidemic at the beginning of the century, is seldom warranted now, for the day has come when the fly and/or the disease, instead of man, can be ousted from a stricken area, if the population is not so sparse and the land so poor that it isn't worth fighting for.

One of the best demonstrations of what can be accomplished was the eradication of tsetse in the Anchau corridor, a strip 70 miles long and 10 miles wide, inhabited by 60,000 people, and its subsequent rehabilitation (see Nash, 1948).

American Trypanosomiases

In the western hemisphere, where there are no tsetse flies, certain species of trypanosomes parasitic in domestic animals, which have become independent of their ancestral hosts, have become established. These include *T. equiperdum*, *T. equinum*, and some closely related forms which may be identical, and *T. vivax* (see pp. 175-177). In addition, however, there are at least two trypanosomes of different type which are parasitic in man and many other animals. These are *Trypanosoma* (or *Schizotrypanum*) *cruzi*, found from southern United States to Argentina and transmitted by many kinds of triatomid bugs; and *T. rangeli* (see p. 174), found in the Caribbean area and transmitted, as far as is definitely known at present, only by species of the genus *Rhodnius*. Trypanosomes probably identical with *T. rangeli* have been reported from Guatemala as *T. guatemalensis* and from Colombia as *T. ariarii*.

TRYPANOSOMA CRUZI AND CHAGAS' DISEASE

Chagas, in 1909, found that in villages in the state of Minas Gerais, Brazil, the thatched-roof houses were infested with large bloodsucking bugs, *Panstrongylus megistus*, called barbeiros, and that these bugs were infected with flagellates which, when inoculated into monkeys and guinea pigs, caused acute infections. On further investigation he found that in the infested houses there were frequent cases, especially among infants and young children, of an acute disease characterized by fever, enlarged glands, anemia, and disturbances of the nervous system. In one of these cases trypanosomes were found in the blood, and in others they were demonstrated by injection of animals.

These trypanosomes, named *Trypanosoma* (or *Schizotrypanum*) *cruzi* (see p. 154), have since been found to parasitize many small mammals, and to be common in bugs of the subfamily Triatominae all the way from the pampas of Argentina to the deserts and canyons of southern California and Arizona, and the scrub woods and farms of southern Texas. A similar parasite has been found in Asiatic monkeys. Fortunately, human infection is less widely distributed.

The Parasite. *Trypanosoma cruzi* is a curved, stumpy trypanosome about 20 μ long, with a pointed posterior end, an elongated nucleus in the center of the body, a large egg-shaped kinetoplast close to or at the posterior end, a narrow and only slightly rippled undulating membrane, and a moderately long free flagellum (Fig. 38).

This species as found in the blood never exhibits stages in division. Greatly swollen cells, enclosing a mass of rapidly dividing parasites,

varying in their number from just a few to many hundreds, are found in tissues of infected man and animals. The parasites multiply thus, especially in cells of the heart and voluntary muscles, central nervous system, and various glands. During the stage of rapid intracellular multiplication the parasites are round in form and resemble leishman bodies (Fig. 39A), but as they grow older a flagellum grows out, and crithidial and eventually trypanosome forms develop (Fig. 39B).

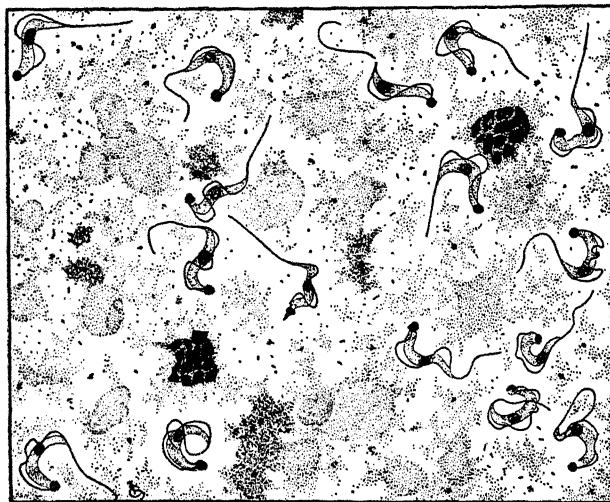


FIG. 38. *Trypanosoma cruzi* in dehemoglobinized thick drop of blood from experimentally infected mouse. (After Brumpt, *Presse méd.*, 1939.)

Then the loaded cell ruptures, liberating the parasites, which invade neighboring cells or are distributed to other parts of the body by the lymph or blood system, unless destroyed by immunological reactions before they reach the safety of another cell. It is only in the early, acute stage of the disease that the parasites can live in the blood for long. In the chronic stage, when antibody reaction has occurred, the blood forms are rarely seen and can be demonstrated only by animal inoculation or culture, although parasites may still be abundant in tissue cells.

T. cruzi is a very versatile trypanosome. Its natural hosts appear to be armadillos, opossums, and rodents; it can thrive in monkeys, marmosets, guinea pigs, rats, rabbits, cats, dogs, and other mammals, but not birds. Lizards become infected by eating infected triatomids, and then serve as a means of infecting other bugs when fed upon by them. Large herbivorous animals such as horses, ruminants, and pigs are

little affected, in contrast to their susceptibility to the African trypanosomes, but Brumpt et al. (1939) found that sheep, goats, and pigs could be experimentally infected, and he thinks that pigs, as well as dogs and cats, may constitute a reservoir of infection, a view later supported by the finding of a naturally infected pig in southern Brazil.

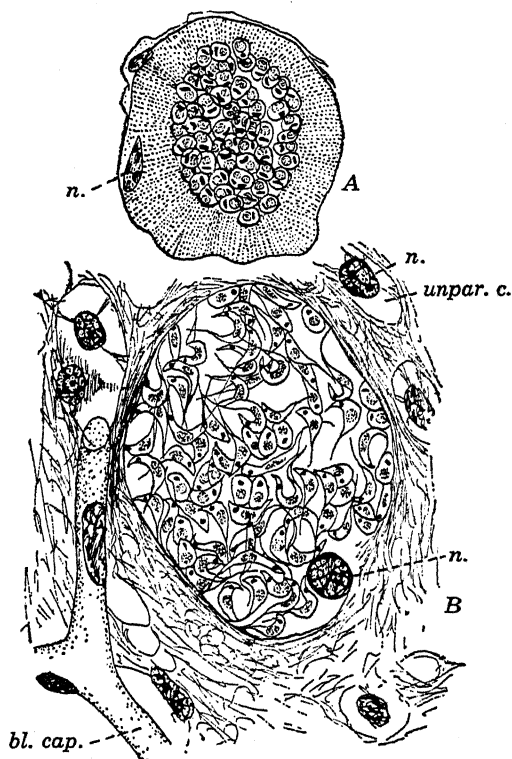


FIG. 39. *Trypanosoma cruzi*. A, cyst containing *Leishmania* forms in muscle fiber of guinea pig, cross section; n., nucleus of muscle fiber. B, older cyst, containing trypanosome forms, in neuroglia cell in gray matter of cerebrum; n., nucleus of parasitized cell; bl. cap., blood capillary; unpar. c., unparasitized cell. $\times 1000$. (After Vianna, Mem. Inst. Oswaldo Cruz, 1911.)

Man seems to be somewhat more resistant to infection than many other mammals. Dias et al. (1945) think that wild animals are not important reservoirs of infection as far as man is concerned, although cats and dogs may be of some importance. Where human infection is common, the transmitting triatomid bugs have adapted themselves to living in houses and the infection is essentially a residential one.

A number of strains of the parasite exist, differing in their infectivity for man. A strain found in bats can seldom be successfully inoculated

into other animals. Mazzoti (1940) isolated a number of strains from triatomids in Mexico which differed in their virulence for guinea pigs. In French Guiana, different strains vary in their infectivity for particular species of triatomids. In arid northeastern Brazil there are many chronic cases, but no acute ones, in contrast to southern Brazil, Paraguay, Uruguay, Argentina, and Chile. The strain found in arid parts of Mexico and southwestern United States also has very low virulence for man, so much so that no cases have been reported from the United States and only eight in Mexico, although man *can* be infected by these strains (see p. 171).

T. cruzi is readily cultured on a variety of artificial media, and is a satisfactory associate for the cultivation of *Entamoeba histolytica* (see p. 85). It develops in chick embryo tissue cultures but not in the embryonic sacs of chick embryos.

Intermediate Hosts, and Transmission. The usual intermediate hosts and transmitters of *T. cruzi* are the large and often highly colored bugs of the subfamily Triatominae, of the family Reduviidae (see p. 589), but this parasite seems not to be very fastidious about the arthropod hosts in which it will develop. Experimentally it develops not only in all species of Triatominae in which it has been tried, but also in bedbugs, *Melophagus*, ticks, and even the body cavity of a caterpillar. In nature, however, the triatomids are probably the only transmitters of any importance. At least thirty-six species of these bugs have been found naturally infected. In southwestern United States and Mexico, about 20 to 25 per cent of bugs are infected, 40 to 60 per cent in Central and South America.

Even of the triatomids, there are relatively few species that are important as transmitters to man; these are the ones that habitually invade houses. These transmitters and their distribution are discussed on p. 594.

The development of *T. cruzi* in the intermediate host (Fig. 40) is similar to that of *T. lewisi* of rats, and takes place in the "posterior station." Within 24 hours the trypanosomes may pass into the intestinal portion of the midgut, where they transform into crithidia and multiply abundantly. Eventually crithidial forms pass to the rectum where small ones are found attached to the epithelium. In the rectum they give rise to "metacyclic" trypanosomes which resemble those in vertebrate blood and are the infective forms. These appear about the sixth day in larval bugs, but not until the tenth to fifteenth in adults. As many as 3500 of these per cubic millimeter may be voided with the insect's excreta.

Normally the salivary glands do not become infective, but S. F.

Wood in 1942 found trypanosomes in great numbers in the body cavity of dead bugs. Probably accidents of some sort caused the body-cavity invasions, which resulted in death of the bugs, but such bugs *might* transmit the infection by their bites before dying.

Transmission usually comes from contamination of mucous membranes or skin with infected excreta. Human infection seems most frequently to come from rubbing the eyes after a bite on the lids, presumably contaminating the mucous membranes or conjunctiva with feces deposited by the bug while feeding, or squeezed out by slapping.

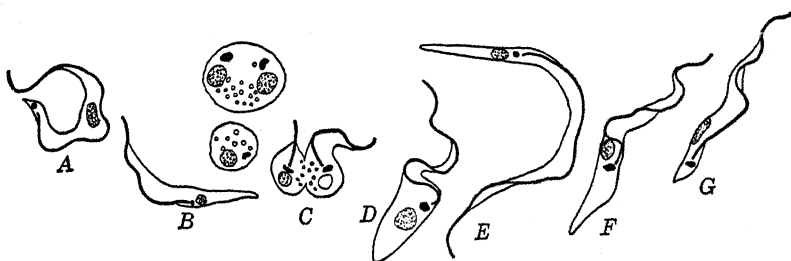


FIG. 40. Development of *Trypanosoma cruzi* in digestive tract of *Rhodnius prolixus*. A, freshly ingested trypanosome; B, crithidia, 6 to 10 hours after ingestion; C, leishmania in midgut, 10 to 20 hours after ingestion; D, redevelopment of flagellum and undulating membrane, 21 hours after ingestion; E and F, crithidia in hindgut, 25 hours after ingestion; G, metacyclic trypanosome in rectum, 8 days or more after ingestion. (A, B, and G adapted from Wenyon, *Protozoology*, 1926; C-F, after Brumpt, *Nouveau traité de méd.*, 1925.)

Animals can become infected by eating the bugs or licking their bites. Cats can be infected by eating infected rodents. The infection can also spread from bug to bug by cannibalism or ingestion of liquid feces (see pp. 594-595). Once infected, a bug remains so probably for the rest of its life.

Human Infection. Human infection with Chagas' disease occurs all the way from Mexico to northern Argentina but is by no means evenly distributed. It is an odd fact that no natural human infections have been observed in the United States, in spite of the fact that *Trypanosoma cruzi* has been found in many species of triatomids in the southwest, from Texas to California, and frequently in a high percentage of individual bugs even in houses (see pp. 593, 594). That the Texas strain is infective for man is indicated by a single successful experimental transmission by Packchanian (1943). In South America the disease is most prevalent in areas where species of triatomids live like bedbugs in houses and habitually suck human blood. Since the bites of triatomids are not infective unless contaminated by the bugs' feces, only constant exposure to bites, especially during sleep, when

they are unconsciously rubbed, is likely to lead to infection, and then only if the bugs regularly defecate during or immediately after a meal, as the "domestic" South American species do. It is possible that the non-domesticated species of triatomids in North America are not as quick to defecate after a meal and are therefore less prone to cause infection. This is known to be true of *T. protracta*.

Only a few cases occur in Mexico and Central America, and little is heard of the disease in Colombia, Ecuador, or Peru. It is common, however, in many parts of Venezuela, French Guiana, Brazil, Bolivia, northern Chile, Paraguay, Uruguay, and northern Argentina. In some areas in Brazil, Bolivia, Chile, and Argentina 10 to 20 per cent of the inhabitants show evidence of infection. In Venezuela Torrealba estimated that there were a million human infections, constituting the principal cause of myocarditis in rural parts of that country, as it apparently does in Brazil. In the northern part of Chile 12 per cent give positive Machado reactions.

There seems to be a rather high natural resistance to acute infections; these occur most frequently in infants and children in whom resistance is weakened by a goiterous condition, malnutrition, or chronic malaria or other chronic diseases. However, acute cases do occur in individuals who are otherwise apparently healthy. The occasional finding of parasites in the blood or by xenodiagnosis in unsuspected cases, high incidence of positive Machado reactions (see p. 173), and frequency of characteristic electrocardiographic changes indicate that the infection is much more frequent than was formerly thought.

When Chagas first discovered human trypanosome infections in the regions of endemic goiter in Minas Geraes, he believed that the goiter, with all its sinister consequences—myxedema, infantilism, cretinism, etc.—was caused by the trypanosome infection, through a supposed toxic effect on the thyroid gland. But it is now evident that Chagas got the cart before the horse—acute trypanosome infections were the result of the goiter, not vice versa.

Prenatal infection has been reported in dogs, and one human case reported by Mazza was apparently acquired with the mother's milk.

The Disease. Acute cases of Chagas' disease are especially common in infants or young children. Frequently the disease begins with an endematous swelling of the eyelids and conjunctiva (Fig. 41) and sometimes other parts of the face, usually only on one side. This is accompanied by inflammation of the tear gland and swelling of lymph glands of the neck. These symptoms suggest that the eye may be the usual site of inoculation, the insect biting the lids, and the victim then rubbing infected excreta from the bug into his eye. The swelling, called

a primary "chagoma," is caused by an inflammatory exudation in the locality where the parasites are colonizing in tissue cells, particularly in subcutaneous fat cells. Later other chagomata may appear in distant parts of the body; they may be conspicuous or only detectable by palpation. During early days of the disease there may be severe headache and marked prostration, with more or less continuous fever. After this acute stage subsides the disease goes into a chronic stage, which many authors believe persists for life, but there may first be a long latent period with few or no symptoms, during which the disease is insidiously progressing. Characteristic symptoms in the chronic stage are extensive, hard edema, inflamed lymph glands, and enlarged liver and spleen. In protracted cases there is a progressive anemia and sometimes nervous disturbances. In severe cases death may occur in two or three weeks.

Disturbance of the heart is very common and according to Chagas is the commonest chronic manifestation in man. Nearly all fatal cases show injury to the heart muscle, which is one of the favorite tissues attacked by the parasite. The injury causes separation of the cells, inflammatory infiltration by phagocytic cells, and increase of fibrous tissue, which weakens the heart in chronic cases. Electrocardiograms show characteristic types of heart blocks and other abnormalities. In Brazil Dias (1953) found heart abnormalities in 16 per cent of electrocardiograms in a place where positive serological tests ran over 50 per cent, but in only 6 per cent in a non-endemic area. Old-age security is a minor problem in areas where Chagas' disease is highly endemic.

Diagnosis. In acute cases a diagnosis can usually be made by finding the parasites in direct blood smears, but in some acute and most subacute cases such slow or tiresome methods as blood cultures, large inoculations of blood into susceptible animals, or xenodiagnosis (feeding of uninfected bugs on the patient) have been resorted to. Muniz, however, showed in the late 1940's that a precipitin test is helpful in such cases, using a polysaccharide extract of cultured trypanosomes as antigen; this method is simple, rapid, and reliable, since no cross-reactions are obtained in leishmaniasis cases. In chronic cases a complement fixation test, called the Machado reaction, is useful; nega-



FIG. 41. Acute case of Chagas' disease in 5-year-old Brazilian girl, with trypanosomes easily seen in blood. (Photograph supplied by Emmanuel Dias.)

tive reactions rule out all but very early stages of infection, and strongly positive results occur only in *T. cruzi* and *Leishmania* infections. The latter can be ruled out by clinical examination or by the formol-gel test (see p. 143), which is not positive in Chagas' disease. The large size of the kinetoplast of *T. cruzi* makes it distinguishable from other trypanosomes in blood smears, and from *Leishmania* in fixed tissues.

Treatment and Prevention. No successful method of treatment is known. Mazza et al. say that Bayer 7602 relieves acute cases, and Pizzi et al. (1953) found Primaquine and an antibiotic, Puromycin, to be helpful by suppressing the parasites temporarily, thus enabling the host to develop resistance. For prevention, good results have been obtained by dusting or spraying with Lindane or Dieldrin. The latter has good residual action. Rebuilding of better houses is being urged everywhere in Brazil, and with good results. The town of Belo-Horizonte, for example, is said to have been nearly freed from Chagas' disease by remodeling of the houses. People accidentally bitten by triatomids, if conscious of it, should avoid possible contamination of the bite by the feces of the bug.

TRYPANOSOMA RANGELI

A trypanosome which is infective for man has been found to be harbored by a considerable percentage of *Rhodnius prolixus* in Venezuela, Colombia, and Guatemala. It was named *T. rangeli* when discovered in *R. prolixus* in Venezuela by Tejera in 1920. Later a parasite which is now considered identical was found in four babies in Guatemala and named *R. guatemalensis*. Later, infections were found in a considerable number of human cases, and also in dogs, in Venezuela, along with *T. cruzi* (Pifano, 1948). In 1951 Groot et al. described what is apparently the same parasite in a large number of people (67 of 183 examined) in the Ariari Valley in Colombia, most of them without *T. cruzi*. They described this trypanosome under the name *T. ariarii*, since at the time they did not feel justified in identifying their species with *T. rangeli*.

These trypanosomes, as they occur in the blood, are characterized by a small kinetoplast, rippled undulating membrane, anteriorly placed nucleus, and large size (see key, p. 156). These parasites develop in the posterior station in *Rhodnius prolixus* and in at least one other species of *Rhodnius*. They produce pyriform, crithidial, and trypanosome forms, distinguishable from comparable stages of *T. cruzi* by the small kinetoplast and the extraordinary length attained by some of the crithidias—32 to 60 μ or more. Although developing in the posterior station and transmissible in the same manner as *T. cruzi*, these trypano-

somes are unique in that they also commonly invade the hemocoel and from there the salivary glands, so that the infection can be transmitted by bite as well as by fecal contamination (Groot, 1952).

T. rangeli is infective for dogs, monkeys, opossums, the anteater, and baby mice. It multiplies in the blood, and no leishmanial tissue stages have been found. Thus far there is no evidence of any pathogenic effects of these trypanosomes.

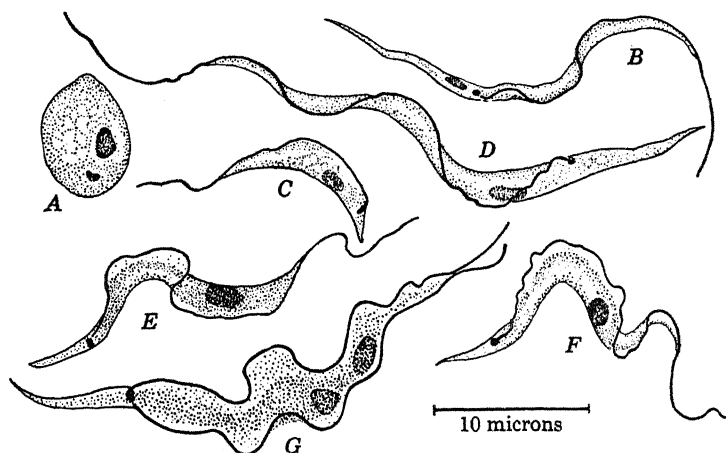


FIG. 42. *Trypanosoma rangeli* (= *ariarii*). A and B, from cultures; C, from anterior part of gut of *Rhodnius*; D, from posterior part of gut of *Rhodnius*; E and F, from human blood; G, dividing form from blood of experimentally infected mouse. (After Groot, Renjifo, and Uribe, *Am. J. Trop. Med.*, 1951.)

Trypanosomiasis of Animals

As noted at the beginning of this chapter, tsetse-borne trypanosome infections, by making it impossible to keep domestic animals, particularly cattle, where even small numbers of tsetse flies are present, have been a tremendous impediment to the development of Africa. Some trypanosomes of animals have become partly or completely independent of tsetse flies, and have become a scourge in parts of the world far distant from the home of the tsetse flies.

SPECIES

There are four groups of trypanosomes that affect domestic animals. (For morphological characters, see key, p. 156, and Fig. 34.)

1. The *brucei* group includes *brucei*, *gambiense*, and *rhodesiense*, which invade the salivary glands of the tsetse fly (Fig. 40) (see p. 158); and also three species that have become independent of their ancestral tsetse hosts: *evansi* and *equinum*, which are transmitted mechanically

by *Stomoxys* and tabanids, or even vampire bats, and are found in all tropical countries; and *equiperdum*, which has gone all the way in becoming independent of insects and depends on venereal transmission.

2. The *congolense* group includes *congolense*, *simiae*, and *dimorphon*, which in the tsetse fly pass forward from the stomach to the labial cavity but do not invade the salivary glands.

3. The *vivax* group includes *vivax* and *uniforme*, which develop only in the proboscis of tsetse, and do not survive in the stomach.

4. *T. theileri* is a large, non-pathogenic species in cattle which develops in the posterior station in tabanids, and *T. melophagium* is a similar parasite of sheep and sheep "ticks," *Melophagus ovinus*.

These species differ in their morphology (see Fig. 34), in their effects on various animal species, and in their response to drugs, as well as in their development in tsetses. The disease caused by the tsetse-borne African species is called nagana; by the mechanically transmitted *evansi*, surra; by *equinum*, mal-de-caderas; and by the venereally transmitted *equiperdum*, dourine.

T. congolense is the most destructive to cattle. It causes a slowly progressing anemia which is nearly always fatal to adult cattle, though calves frequently recover and have "cryptic" infections. Horses, sheep, goats, camels, and dogs are also susceptible, but pigs are very little affected. Strains of the parasite and adequacy of nutrition of the host are important factors in determining the outcome of this as of the other trypanosome infections. This species lives its whole life in the capillaries, producing its effects almost entirely by blocking capillaries and causing anemia.

T. simiae causes acute, rapidly fatal infections of pigs and camels, is chronic in monkeys, but is of little importance to other animals. This species produces disease in the same way as *congolense*.

T. brucei causes a very serious and usually fatal disease of horses, sheep, goats, camels, and dogs, but a very mild disease in cattle. This parasite injures the walls of capillaries and passes through into the intercellular tissue spaces; no organ is immune from its damage.

T. vivax, unlike those mentioned above, although cyclically transmitted in tsetses, can survive outside tsetse fly areas, where it depends on mechanical transmission by *Stomoxys* and tabanids; it has become established not only in tsetse-free areas in Africa, but also in tropical America. It causes disease in all large domestic animals except dogs, but different strains vary greatly in their pathogenicity, from rapidly fatal infections to chronic or cryptic ones. Like *brucei*, it leaves the capillaries and invades the tissues. The related *T. uniforme* is very much like *vivax*, but seems to be relatively harmless to sheep and goats.

T. evansi, the cause of surra, is essentially a disease of camels, but it also causes acute and fatal disease in horses and dogs, chronic in donkeys, and transient in cattle. Its effects are quite similar to those of *brucei*, from which it and *equiperdum* have doubtless both been derived. *T. equinum* and some related or identical forms in South America are probably mere strains of *evansi* which have lost the kinetoplast (see p. 154).

T. equiperdum is the cause of dourine, a venereal disease of horses. In addition to the anemia, edema, and wasting caused by all forms of trypanosomiasis in animals, this one causes acute inflammation and edema of the penis and vagina, and plaque-like skin eruptions.

Treatment and Prophylaxis. Formerly animals were treated, with only fair success, with antimony compounds and antrypol, but in recent years two new drugs, dimidium bromide (phenanthridium), and Antrycide in the form of methyl sulfate or chloride salts, have greatly brightened the picture. Antrycide is not equally effective for all the species of trypanosomes, being much more effective against *congolense* than against *vivax*, somewhat less against *brucei*, *evansi*, and *equiperdum*, and rather ineffective against *simiae*. However, in tolerated doses of 5 mg. per kilo of the more soluble methyl salt it is curative for cattle and horses, and in the less soluble chloride form a single dose gives protection against infection for 2 to 8 months. A mixture of the two salts, called a "pro-salt," given subcutaneously combines therapeutic and prophylactic virtues; it has been claimed, however, that the effect of the drug is suppressive rather than prophylactic. Dimidium bromide is more expensive but is effective in smaller doses (1 to 1.5 mg. per kilo), but in some animals it causes photosensitization and is ineffective against *brucei*, *evansi*, and *simiae*.

These drugs are especially valuable when animals are temporarily exposed to fly infections, e.g., in transit through fly belts, dry-season grazing in fly areas, or in connection with clearance schemes where tsetse are seasonally present.

One of the darkest clouds on the horizon now is the fact that Antrycide-resistant strains of trypanosomes, particularly of *congolense*, can and do develop, which may in time destroy the dream of Africa as a vast new home for contented cows.

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The Sporozoa

I. Malaria

The Sporozoa include a large and varied assemblage of Protozoa which have little in common except a parasitic mode of life, the lack of any organs of locomotion during most stages of their development, and the evolution of a complicated life cycle usually involving an alternation of generations and the production of resistant stages which in some cases are called spores. There is little foundation to support the inclusion in a single group of such diverse parasitic organisms as the Coccidia, haemoflagellates, and gregarines, constituting the class Telosporidea; the Myxoporida and Microsporida, parasites of fishes and arthropods, constituting the class Cnidosporidea; and the Haplosporidia, inhabiting many hosts from rotifers to fishes. Even *Rhinosporidium* and the Sarcosporidia, now commonly considered as fungi, were once included in this hodgepodge group. However, since most protozoologists prefer a single conglomerate mess to several groups of very uncertain relationships, we shall follow along and include all these varied organisms in the subphylum Sporozoa (see p. 41).

Classification

All the parasites which concern us here fall in the class Telosporidea, which, following Jahn and Jahn, and Hall, we shall classify in this way:

Class **Telosporidea** (for characteristics, see p. 41).

Subclass 1. **Gregarinidia**. Typically parasites of digestive tract and body cavities of invertebrates, where trophozoites usually live free, generally as elongated, spindle-shaped organisms. These eventually form gametocytes either by direct transformation or after one or more schizogonic multiplications. Gametocytes associate in pairs, undergo syngamy, and then usually encyst, forming an oöcyst in which sporozoites are produced. The oöcyst or "spore" is the usual means of transfer.

Subclass 2. **Coccidiida**. Typically parasites of epithelial cells of invertebrates and vertebrates, intracellular throughout most of the life cycle. Sporozoites, naked or in sporocysts or oöcysts, are ingested and enter tissue cells, where they multiply by repeated schizogony. Last genera-

tion of merozoites develop into gametocytes. These form dissimilar gametes which undergo syngamy, forming zygotes enclosed in cysts (oöcysts) which do not grow in size. In these sporozoites are produced, usually in intermediate products of multiplication, the sporocysts. Intermediate host may or may not be involved.

Order 1. **Adeleida**. Gametocytes dissimilar, associated during development; microgametes few. Two suborders: (1) *Adeleina*, with inactive zygote and non-growing oöcysts; includes parasites of invertebrates and one, *Klossiella*, of mice and guinea pigs. (2) *Haemogregarinina*, with motile zygotes and growing oöcysts in an intermediate host. *Haemogregarinina* undergoes schizogony in fixed cells and gametocytes (Fig. 43L) enter erythrocytes of turtles or snakes, sexual phase in leeches. In *Hepatozoön* the gametocytes enter leucocytes of birds or mammals (Fig. 43K), and the sexual phase is in arthropods.

Order 2. **Eimeriida**. Gametocytes similar, not associated during development; microgametes numerous. Fertilization in oöcysts; latter do not grow, but produce sporozoites, usually in sporocysts. Most have no intermediate hosts. Includes the Coccidia of vertebrates (family Eimeriidae) (see pp. 219–226).

Subclass 3. **Haemosporidia**. Schizogony in fixed tissue cells, with or without subsequent schizogony in erythrocytes. Gamonts or gametocytes in red or white blood cells. Fertilization in arthropod host. Zygote motile; oöcyst grows and produces many sporozoites. Asexual phase in lizards, birds, or mammals, sexual phase in arthropods:

Order 1. **Plasmodiida**. Gametocytes in blood cells of vertebrates; formation and syngamy of gametes in arthropod host; pigment granules deposited when red cells invaded. Includes true malaria parasites (*Plasmodium*), and allied genera such as *Haemoproteus* and *Leucocytozoön*.

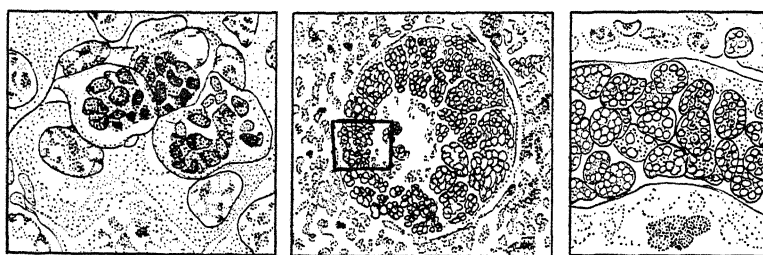
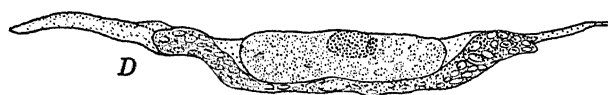
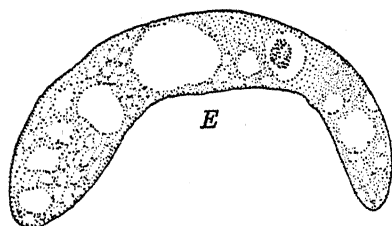
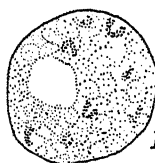
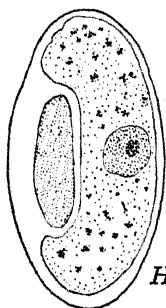
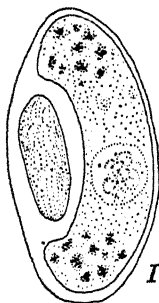
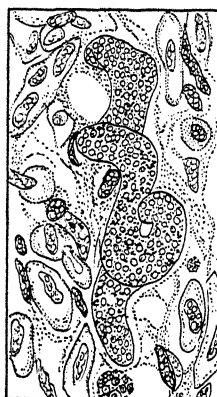
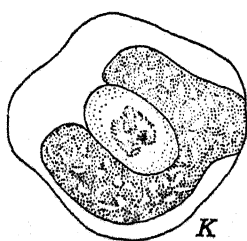
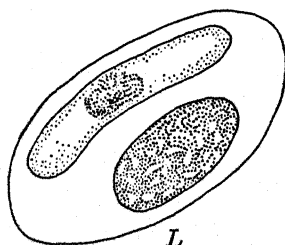
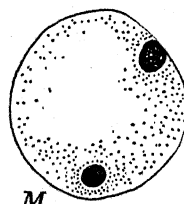
Order 2. **Babesiida**. Unpigmented forms in red corpuscle, dividing into groups of 2 or 4, rarely more, these probably being gamonts, which develop into gametocytes and produce gametes in ticks; with or without schizogony in various vertebrate tissues. Life cycles imperfectly known. Contains one family, Babesiidae, with the genera *Babesia*, *Theileria*, and other genera parasitic in mammals and birds (see p. 213).

Of uncertain status: *Toxoplasma* (p. 216).

Until recently the Sarcosporidia were included in the class Acnidosporidea (see p. 41), but Spindler (1945) gave evidence that they were not Protozoa but fungi, a disposition which has also been suggested for *Toxoplasma*. Formerly another group of minute parasites of blood corpuscles—*Bartonella*, *Anaplasma*, *Eperythrozoon*, and a few others—was included in the Protozoa, attached as “riders” to Haemosporidia, but these are no longer regarded as Protozoa (see p. 230).

Classification of Malaria-like Parasites

In the present chapter we shall consider only the malaria parasites and their allies, i.e., the order Plasmodiida as given above. This group includes numerous parasites which occur in lizards, birds, and cer-

*A**B**C**D**E**F**G**H**I**J**K**L**M*

tain mammals. Primates, rodents, shrews, and bats are the mammals thus far known to harbor them. Only members of the genus *Plasmodium*, which includes the human malaria parasites, undergo schizogony in red blood cells; the others undergo this multiplication only in fixed or (in bat malaria) in fixed and wandering macrophages. Before the exo-erythrocytic (e.e.) stages of *Plasmodium* became recognized as essential parts of the life cycle, this genus was segregated into a separate family of its own (Plasmodiidae) and the others grouped in a family, Haemoproteidae, but there no longer seems justification for this. Attempts to classify these organisms on the basis of type of exo-erythrocytic development or of their arthropod hosts have not been successful either.

At the present, we may recognize the following genera:

1. ***Plasmodium***: parasites of lizards, birds, and mammals; gametocytes in red cells; erythrocytic schizogony; e.e. forms in various tissues, but always solid or at most vacuolated bodies (Fig. 47); arthropod hosts mosquitoes (*Anopheles* for mammalian species; culicines, or rarely *Anopheles*, for bird and lizard species).

2. ***Leucocytozoön***: parasites of birds; no erythrocytic schizogony; gametocytes in round or elongated lymphocytes or red cells (Fig. 43D); e.e. forms (Fig. 43A-C) in parenchyma of liver, heart, or kidney, forming large bodies divided into cytomeres; arthropod hosts, as far as known, blackflies (*Simulium*), with development in stomach (Fig. 43E-G).

3. ***Haemoproteus***: parasites of birds and reptiles; no erythrocytic schizogony; gametocytes halter-shaped in red cells (Fig. 43H, I); e.e. forms in endothelium of blood vessels, especially in lungs (Fig. 43J); arthropod hosts, as far as known, Pupipara.

4. ***Hepatocystes***: parasites of lower monkeys and squirrels; no erythrocytic schizogony; gametocytes in red cells; e.e. forms cyst-like, very large, in liver parenchyma; arthropod hosts unknown.

5. Species assigned to *Plasmodium* until more is known about them: parasites of bats and elephant shrews; no erythrocytic schizogony; gametocytes in red cells; e.e. forms in one bat species in fixed and wandering macrophages and reticular cells of bone marrow; arthropod hosts unknown.

Malaria and Malaria-like Diseases in Animals Other than Man

Haemoproteus Infections. The elongated, halter-shaped gametocytes (halteridia) (Fig. 43H, I) of species of *Haemoproteus*, curving

FIG. 43. Miscellaneous blood-inhabiting organisms. (Adapted from various authors.)

Leucocytozoön simondi, A-G: A, early developing schizont in liver of duck, $\times 1640$; B, later stage of megaloschizont in liver of duck, $\times 410$; C, enlarged portion of B, $\times 1180$; D, gametocyte in duck blood, $\times 1640$; E, oökinete in stomach of *Simulium* (magnification not given); F, oöcyst in stomach, $\times 2500$; G, sporozoites, $\times 2500$, also in stomach.

Haemoproteus columbae, H-J: H and I, \varnothing and δ gametocytes, respectively, in pigeon erythrocytes; J, schizont in lung capillaries of pigeon.

Hepatozoön muris, K: gametocyst in mononuclear leucocyte of rat.

Haemogregarina sp., L: gametocyte in erythrocyte of turtle (differs from *Haemoproteus* in having no pigment granules).

Anaplasma marginale, M: in erythrocyte of cattle.

around the nuclei of the red blood cells, have been found in the blood of numerous species of birds (see Herman, 1944). One species, *H. columbae*, is very common in pigeons, although it does not do them very much harm. The life cycle of only two species have been worked out, and in both cases pupiparous flies of the family Hippoboscidae (see p. 688) serve as intermediate hosts, although on epidemiological grounds it is suspected that there may be other vectors.

Leucocytozoön Infections. The gametocytes of *Leucocytozoön* (Fig. 43D) also are found in the blood of many species of birds. Two species, *L. simondi* (= *anatis*) of ducklings and *L. smithi* of turkeys, cause serious losses. The schizogony stages are of two kinds—small schizonts in parenchyma cells of the liver (Fig. 43A) and “megalo-schizonts” (Fig. 43B,C) up to over 150 μ long, and containing over a million merozoites, in the heart, liver, and spleen in macrophages and heart muscle. The intermediate hosts are species of blackflies (Simuliidae). In the case of *L. simondi*, at least, the whole sexual cycle, including development of the sporozoites (Fig. 43, E-G), usually occurs in the stomach instead of on its outer wall, and the salivary glands are not commonly invaded (see Fallis et al. 1951).

Plasmodium Infections of Lizards and Birds. The bird parasites of the genus *Plasmodium* are of particular interest because of their extensive use in the study of the biology and treatment of malarial parasites in general. Until the discovery of *P. berghei* in rodents in 1948, bird malaria had to be depended upon to a large extent for screening anti-malarial drugs, since monkeys were too few and too expensive to be used on such a large scale. It was in *P. gallinaceum* of chickens that exo-erythrocytic stages were found to be an essential part of the life cycle of malaria parasites.

The majority of the species of *Plasmodium* of birds are, primarily at least, parasites of passerine birds; such are *relictum*, *cathemerium*, *elongatum*, *circumflexum*, and many others, but *gallinaceum* is primarily a parasite of galliform birds and *lophurae* of some galliform birds and of ducks. Huff et al. (1947) showed that the behavior of these various parasites differs considerably in different hosts, so that it may not be easy to decide which are the natural ones. In unnatural hosts there may be no development at all; more or less suppression of either the blood or exo-erythrocytic stages or both; failure to produce gametocytes; or lack of sexual potency of the gametocytes. Interesting examples of these conditions have been given by Huff and Coulston (1946) and by Huff, Coulston, Laird, and Porter (1947). The bird species are transmitted by various species of *Aedes* and *Culex*, and rarely by *Anopheles*.

There are two types of development of e.e. forms: the commoner *gallinaceum* type in which they develop in the fixed cells (macrophages and endothelial cells) of the brain, spleen, lung, and many other organs; and the *elongatum* type in which they develop in cells of the blood-forming organs and circulate in both red and white blood cells. In lizards, which harbor a number of species, both types of development occur, at least in some species.

Mammalian Species of Plasmodium. Typical species of *Plasmodium*, i.e., those which undergo schizogony in the red blood cells and are transmitted by mosquitoes, are found among mammals only in man and monkeys with the exception of two related species, *P. berghei* and *P. vinckei*, found in African rats and transmissible to various rodents. Both the primate and rodent parasites are transmitted by species of *Anopheles* only.

Apes and monkeys harbor a number of species, some of them so closely related to the species found in man that there is question about their distinctness. It is very likely that *P. rodhaini* of chimpanzees is identical with *P. malariae* of man. *P. cynomolgi*, which is very similar to *P. vivax*, has proved very useful in studies on the e.e. cycle, and also on drugs. *P. knowlesi*, which causes rapidly fatal infections in rhesus monkeys, causes relatively mild and temporary infections in man, and was once used for malaria therapy of syphilis. *P. berghei* is now being used experimentally in the study of mammalian malaria, but it does not show as close an affinity to the human species as the monkey parasites do.

An interesting light was thrown on host-parasite relations of malaria parasites by the observation that whereas rats are easily infected by either blood or sporozoite inoculation with *P. berghei*, mice can be infected only by blood inoculation, showing that the conditions for the erythrocytic and exoerythrocytic cycles may not be parallel in different hosts.

Human Malaria

History and Importance. Malaria, meaning bad air, was so named because of association of the disease with the odorous air of swamps, particularly at night, and fear of damp night air still exists, even in the United States. Although historians and economists have largely failed to recognize it, malaria must have played a large part in the history of the world and the progress of nations.

The malaria parasite was discovered in the blood by Laveran in 1880. In 1898 Ross experimentally proved the mosquito transmission of the disease, and worked out the details in the case of bird malaria.

Immediately afterward Grassi and his pupils, working independently, described the cycle of human malaria in *Anopheles*.

Although malaria probably still ranks, as of this writing, as the number 1 human disease from the point of view of prevalence and the mortality, sickness, and economic loss it produces, present prospects are that this statement cannot be made in further editions of this book, for malaria today is definitely sick. Up to the end of World War II there were estimated to be 350,000,000 cases annually, 1 per cent of them fatal. Malaria is still present in all tropical and subtropical parts of the world, except in some of the Pacific islands (Hawaii, Fiji, New Caledonia) where there are no *Anopheles* mosquitoes, but as an endemic disease it has been practically or completely banished from the continental United States, and from parts of Europe (including Italy, where it probably contributed to the fall of the Roman Empire, Sardinia, and parts of Greece). In South America, Chile has been free of malaria for years, and in parts of many other countries the disease is dead or dying.

Even in such notoriously malarious areas as parts of Africa, India, and Ceylon, vast strides have been made in the control of this disease. In Ceylon, reduction has had the dramatic effect of arousing pessimistic warnings about liberation from disease without preparation for a balanced economy, which, they say, may as well lead to overpopulation, unemployment, communism, and war, as to peace, prosperity, and contentment. But as Russell (1951) ably pointed out, withholding public health cannot possibly restore a balance that never existed in the past, and cannot in the future *without* public health.

During World War II malaria was the number 1 problem of non-immune troops and caused tremendous havoc in the Mediterranean, India-Burma, and South Pacific theaters of operation. At the fall of Bataan, when quinine ran out, 85 per cent of every regiment had acute malaria. In the South Pacific campaign, malaria caused more than five times as many casualties as did combat. In April 1942, the case rate on Efati was 2678 per 1000 per year, and on Guadalcanal in November 1942, two months after occupation, the rate was 1800 per 1000 per year. That was before the importance of malaria was realized, and before strict malaria discipline was developed. The prevalent attitude then was well expressed by one high-ranking officer who said, "We are out here to fight Japs, and to hell with mosquitoes." That was a good slogan, but not the way the officer meant it. When it became apparent that malaria had to be licked before the Japs could be, the job was successfully done by the combined efforts of entomologists, sanitarians, engineers, physicians, and occasional court martials,

and malaria rates dropped to 10 to 50 per 1000 in some of the world's worst malarial areas.

Malaria in the United States. Opinions differ as to whether malaria existed in America in pre-Columbian days, but it developed soon thereafter and was a scourge during colonial and pioneering days. Of 45,713 patients admitted to Charity Hospital in New Orleans from 1814 to 1847, 43 per cent were classed as "fevers" and 20 per cent as "intermittent fevers." In the Civil War one command of 878 men below Savannah had 3313 cases of malaria in 14 months!

During earlier days in this country malaria was prevalent in the northern and midwestern states as well as in the South, but it died out there about the turn of the century, largely as the result of agricultural drainage, treatment, screening, better hygiene, and household spray guns. These factors were reducing the disease in the South, but there the process was greatly hastened by the development of a DDT residual-spraying program. Civilian malaria mortality decreased over 90 per cent between 1935 and 1945, and in the early 1950's malaria ceased to exist as an endemic disease in continental United States. In 1951 the National Malaria Society voluntarily ceased to exist because its goal had been attained—surely a unique occurrence in public health history!

Species of *Plasmodium* in Man. Four species of *Plasmodium* are capable of causing malaria in man. One, *P. ovale*, is very rare, though it has been found in such widely separated parts of the world as West Africa, South America, Russia, Palestine, and New Guinea. The other three species, *P. vivax*, *P. malariae*, and *P. falciparum*, are common and of wide distribution.

P. vivax is the commonest and most widely distributed species, being prevalent in both tropical and temperate zones. It is the cause of "tertian" or "benign tertian" malaria, though a better term is "vivax" malaria. It has a 48-hour cycle of development in man and is particularly likely to cause relapses. *P. malariae* is also widely distributed in both tropical and temperate climates, but it has a spotty distribution and is usually much less common than either *vivax* or *falciparum*. It is the cause of "quartan" malaria. It has a 72-hour cycle and causes infections of many years' duration. *P. falciparum* is very prevalent in the tropics but does not thrive as far north as *vivax* does. It has a 40- to 48-hour cycle of development and is the cause of "malignant tertian," "subtertian" or "aestivo-autumnal" malaria, now preferably called "falciparum" malaria. It causes a much more dangerous disease than the other species but runs a shorter course without relapses, seldom lasting more than 8 to 10 months without reinfection. The principal

morphological and physiological differences between the human species are indicated in the table on p. 189 and in Figs. 44 and 45.

In at least two of the human species, *vivax* and *falciparum*, there are races or strains differing in their clinical course, geographic distribution, and ability to produce immunity to each other.

There is no animal reservoir for any of these human parasites except possibly chimpanzees for *P. malariae*. Malaria cannot, therefore, be acquired in uninhabited regions; for malaria to thrive there must be infected human beings and plenty of man-biting *Anopheles*, and easy contact between the two.

Life Cycle. Although the general nature of the life cycle of all species of *Plasmodium* is similar, there are some marked differences between them which have very important practical consequences. The general course of the life cycle is shown in Fig. 46. Although partly hypothetical, the circumstantial evidence for its correctness is very strong.

EXO-ERYTHROCYTIC STAGES. When sporozoites are injected by a mosquito they do not enter erythrocytes at once to start their development. Within a few minutes after injection they leave the blood stream and enter tissue cells where they go through at least two schizogonic cycles before invading the blood. The first generation of these pre-erythrocytic tissue parasites are called by Huff "cryptozoites"; the following ones he calls "metacryptozoites." The parasites then invade the blood stream and enter erythrocytes, but in some species, at least, the exo-erythrocytic forms may continue to multiply indefinitely. In some bird species in favorable hosts, when erythrocytic parasites are injected instead of sporozoites, some of these may penetrate the tissues and become exo-erythrocytic. To distinguish these from the pre-erythrocytic forms Huff and Coulston (1946) use the term "phanerozoites," but obviously, except at the beginning of an infection, there would be no way of distinguishing exo-erythrocytic forms derived from sporozoites from blood forms that had reverted to an exo-erythrocytic life. The exo-erythrocytic forms do not have pigment granules in them.

Although easily studied in bird malaria, especially in *P. gallinaceum* infections, the exo-erythrocytic stages long escaped detection in monkeys and man. It was, however, certain that they existed, since the sporozoites disappear from the blood stream 30 minutes after inoculation and continue to hide out until 6 days later in *vivax* infections and 8 days in *falciparum* infections. Shortt et al., in 1948 succeeded in finding the schizonts in the parenchyma cells of the liver of a rhesus monkey after very heavy inoculation with sporozoites of *P. cynomolgi* and subsequently found the pre-erythrocytic schizonts of *P. vivax* in the liver

COMPARISONS BETWEEN ERYTHROCYTIC FORMS OF DIFFERENT SPECIES OF HUMAN MALARIA PARASITES

Human Malaria

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	<i>P. vivax</i>	<i>P. malariae</i>	<i>P. ovale</i>	<i>P. falciparum</i>
Rings.	Coarse, about $\frac{1}{4}$ to $\frac{1}{2}$ diameter of corpuscle; rarely more than one in corpuscle.	Similar to <i>vivax</i>	Similar to <i>vivax</i> ; Schüffner's dots may be present even in this stage.	Fine, about $\frac{1}{4}$ to $\frac{1}{2}$ diameter of corpuscle; doubly infected corpuscles common; often situated at edge of corpuscle; two nuclei frequent.
Corpuscles infected with schizonts.	Enlarged and pale; contain Schüffner's dots.	Size and color normal; no Schüffner's dots.	Oval in shape, often fimbriated; not much enlarged; normal in color; contain Schüffner's dots.	Not seen in peripheral circulation; size normal; color dark, brassy; have reddish clefts called Maurer's dots, and may have bluish stippling.
Growing schizonts.	Very irregular, sprawled out over cell; pigment in small brown granules, usually collected in a mass.	More compact and rounded, or drawn out band-like across cell; pigment blacker and in coarser granules.	Usually round, not ameboid; pigment brownish, coarse, somewhat scattered.	Usually compact, rounded; pigment coarse and blackish; not seen in peripheral circulation.
Segmenters.	Nearly full enlarged, dotted corpuscle; 15 to 20 merozoites, occasionally up to 32, irregularly arranged.	Nearly full normal-sized corpuscle; 6 to 12 merozoites, commonly 8 or 9, arranged like daisy head.	Occupy $\frac{1}{4}$ of dotted oval corpuscle; 8 to 10 merozoites, arranged like bunch of grapes.	Occupy $\frac{1}{4}$ to $\frac{1}{2}$ of corpuscle; number of merozoites very variable, from 8 to 32, not seen in peripheral circulation.
Gametocytes.	Rounded, larger than corpuscles ($10-14 \mu$ in diameter); pigment granules fine, brown, evenly peppered throughout cytoplasm.	Rounded, smaller, nearly filling a corpuscle of normal size; pigment blacker and coarser than in <i>vivax</i> and more or less concentrated at center and periphery.	Rounded, filling $\frac{1}{4}$ of enlarged dotted corpuscle; pigment coarse, black, evenly peppered.	Crescent-shaped or bean-shaped with pigment granules clustered about nucleus at center; remnants of corpuscle often not in evidence.
Distinctions between microgametocytes and macrogametocytes.	Microgametocytes with pale cytoplasm; nucleus large, pink, often stretched across center of body. Macrogametocytes slightly larger, with deeper blue cytoplasm; nucleus small, red, usually lying at or near one side of body.	Same differences as in <i>vivax</i> .	Same differences as in <i>vivax</i> .	Microgametocytes short and squat with pale blue cytoplasm and pink nucleus; pigment granules scattered except at poles. Macrogametocytes longer and more slender, deeper blue, with small red nucleus; pigment more concentrated near center.
Interval between sporulations.	48 hours.	72 hours.	48 hours.	48 hours.

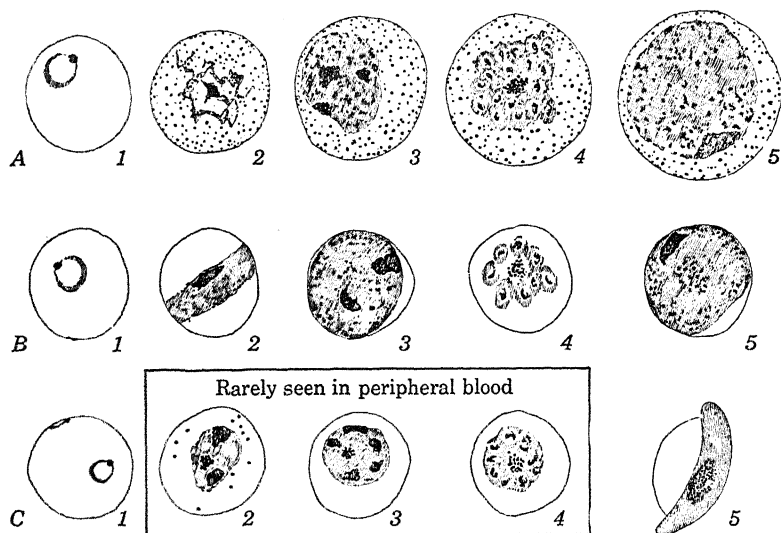


FIG. 44. Comparison of three common species of malaria parasites, illustrating diagnostic characteristics in each stage. A, *Plasmodium vivax*; B, *P. malariae*; C, *P. falciparum*; 1, "ring" stages; 2, growing schizonts; 3, grown schizonts with dividing nucleus; 4, segmenting parasites nearly ready to leave corpuscle; 5, female gametocytes.

of a heavily infected human volunteer. In 1951 Shortt et al. similarly demonstrated the pre-erythrocytic forms of *P. falciparum*, a finding which was confirmed by American workers (Jeffery et al. 1952) after dosing a volunteer with enough sporozoites to be equivalent to 20,000

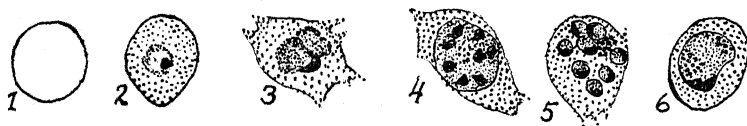


FIG. 45. *Plasmodium ovale*: 1, normal corpuscle. 2, ring stage; note corpuscle already full of Schüffner's dots. 3, young schizont; note irregular shape of corpuscle and "fimbriated" appearance, also seen in 4 and 5. 4, dividing schizont; note oval, fimbriated corpuscle and round parasite. 5, segmenter; note only 8 merozoites around a central clump of pigment. 6, female gametocyte; note similarity to quartan gametocyte except for shape of corpuscle and presence of Schüffner's dots. (Drawn from figures by James, Nicol, and Shute, *Parasitology*, 25, 1922.)

infective mosquito bites. More recently Garnham et al. have demonstrated pre-erythrocytic forms of *P. ovale*, also, in the human liver. The pre-erythrocytic schizonts of *P. falciparum* (Fig. 47) are large lobulated bodies containing some 40,000 minute merozoites, liberated

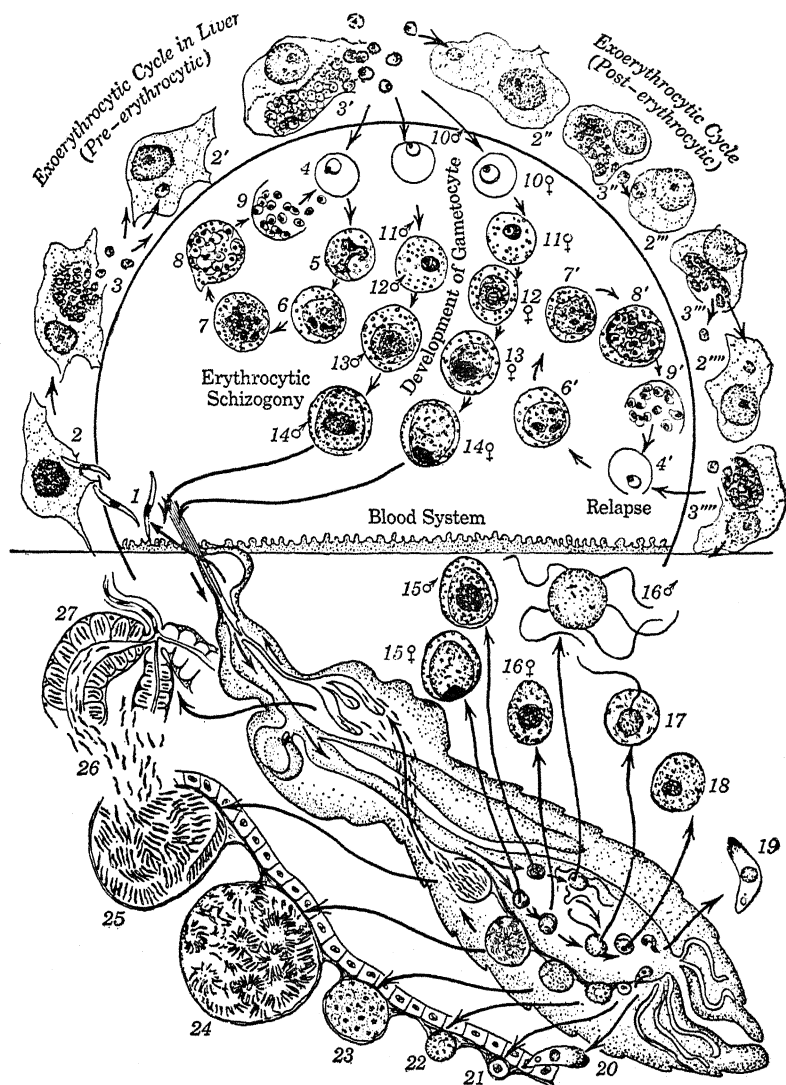


FIG. 46. Life cycle of *Plasmodium vivax*, partly hypothetical. 1, sporozoites injected; 2, sporozoites entering liver cell; 3, exo-erythrocytic schizogony; 4-9, erythrocytic schizogony, repeated indefinitely; 10-14, development of ♂ and ♀ gametocytes; 4'-9', reinvasion of blood by exo-erythrocytic merogony, causing relapse; 15, ♂ and ♀ gametocytes in stomach of *Anopheles*; 16♀, female gamete; 16♂, formation of male gametes by exflagellation; 17, fertilization; 18, zygote; 19, oökinete; 20, same, penetrating stomach wall; 21-25, development of oöcyst (23 shows sporoblasts, 24 and 25 development of sporozoites); 26, sporozoites liberated into body cavity when oöcyst bursts; 27, sporozoites collecting in salivary gland cells and ducts.

only 6 days after infection. Those of *cynomolgi* and *vivax* are smaller, have only about 1000 merozoites, and take 8 days to develop.

The later history of *falciparum* infections suggests that in this species all the parasites are expelled into the blood within a few weeks; when the blood infection is destroyed by drugs no relapse occurs. In *vivax* and *malariae* infections, on the other hand, the exoerythrocytic forms seem to persist, causing relapses when a falling off in immunity or drug treatment makes it possible for them to reinvade the blood stream. In some strains of *P. vivax*, however (see p. 198), there is a long latent

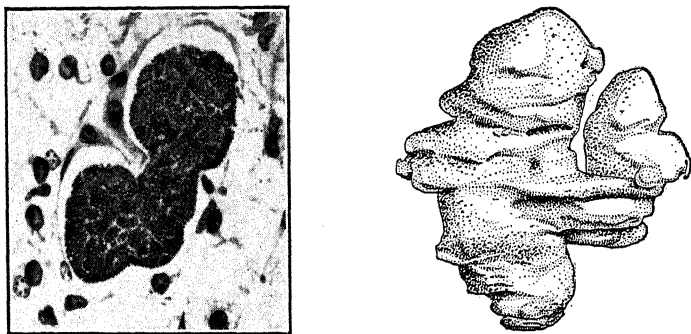


FIG. 47. Left: Pre-erythrocytic schizont of *Plasmodium falciparum* in human liver 6 days after infection by mosquito bites. Right: Reconstruction of a mature schizont. (From figures by Shortt et al., *Trans. Roy. Soc. Trop. Med. Hyg.*, 44, 1951.)

period of many months between the primary attack, which sometimes fails to develop at all, and the first relapse, apparently due to failure of the parasites to try to invade the blood stream rather than to any barrier caused by immunity.

Apparently in *vivax* infections the erythrocytic forms do *not* revert to exo-erythrocytic life as they do in *gallinaceum* infections in birds, for in *vivax* infections induced by blood inoculation no relapses occur once the blood parasites are destroyed.

ERYTHROCYTIC STAGES. About a week or ten days after mosquito infection the parasites invade erythrocytes and begin a process of schizogony. The earliest form of the parasites seen in the corpuscles is the "ring stage" (Fig. 44, 1). It appears like a little signet ring caused by the presence of a transparent or vacuolated area in the center of the parasite, surrounded by a delicate ring of cytoplasm and a tiny nucleus at one side, like the setting in a ring. With the usual blood stains (Giemsa or Wright) the cytoplasmic ring stains blue and the nucleus ruby-red. The rings of *vivax*, *malariae*, and *ovale* are about

one-third the diameter of the blood cells and are indistinguishable, but those of *falciparum* are only about half this size, have hair-like rings, and tend to be perched on the periphery of the corpuscles; corpuscles containing two or more rings are common.

As the parasite grows larger it becomes rounded or irregular in shape. In *Plasmodium falciparum* the infected corpuscles at this stage become viscid and clump together in internal organs and are not seen in the peripheral circulation, but those of the other species continue to circulate in the peripheral blood in all stages. As noted in the table on p. 189, *vivax* infections are indistinguishable in all stages beyond the rings by the enlarged, pale corpuscles which they occupy, studded with red-staining granules called "Schüffner's dots" (Fig. 44A, 2-5). Similar dots appear in *ovale* infections, but the infected corpuscles are oval and not enlarged (Fig. 45). No such dots appear in *malariae* infections, and the infected cells fail to enlarge or grow pale. In *falciparum* infections the infected cells (located in internal organs) may have large, irregular reddish clefts called "Maurer's dots"; they have a darker "brassy" color and may also have a bluish stippling.

As the parasites grow, the nucleus divides into two, then four, and eventually more parts. As maturity approaches, the nuclei tend to take up peripheral positions in the schizont, and a small portion of the cytoplasm concentrates around each. These *segmenters* eventually break free from the corpuscles in which they have developed, and the individual *merozoites* thus liberated attack new corpuscles and repeat the process. The numbers of merozoites in the different species is shown in the table.

The merozoites of *vivax* attack almost exclusively the young immature corpuscles (reticulocytes) and those of *malariae* the older ones, but *falciparum* indiscriminately enters any that are handy. The result is that *vivax* parasites are seldom found in even 1 per cent of the corpuscles and *malariae* in seldom more than 1 in 500, whereas *falciparum* may infect 10 per cent or more, with dire results.

The pigment and other waste products left behind when the parasite breaks up are released into the blood stream and deposited in the spleen or other organs, or under the skin, causing the sallow color so characteristic of malarial patients. It is at the time of the bursting of corpuscles and release of waste products that the characteristic paroxysms of chills and fever are felt.

The species differ in the time they take to mature. *P. vivax*, *ovale*, and *falciparum* take about 48 hours in which to complete the schizogonic cycle, whereas *P. malariae* takes 72 hours, whence the names tertian and quartan. These are derived from the old Roman method of figur-

ing, which counts the day on which something happens as the first day, the second day following being therefore the third (tertian) and the third following day the fourth (quartan). Although the schizogonic cycles of the human species are all 48 or 72 hours, the paroxysms, particularly in early stages of *vivax* and *falciparum* infections, commonly occur daily (quotidian), presumably because the exo-erythrocytic forms enter the blood at various times and consequently different broods mature on different days. The liberation of merozoites does not take place at all hours, however, but is timed by some physiological condition in the host and is largely concentrated within a few hours on each day. In *falciparum* infections the sporulation of all the parasites is less closely synchronized than in the other species, resulting in longer drawn out paroxysms of chills and fever.

After a few generations of schizonts have been produced in the blood some of the merozoites have a different destiny. They grow more slowly, produce more pigment, and develop into large single-nucleated organisms. These are the gametocytes, which continue to circulate in the blood for at least a number of weeks, but undergo no further development within the human body. The gametocytes of *falciparum* are crescent shaped, whereas those of the other species are rounded. Distinguishing characters of the gametocytes of the different species and of the males (microgametocytes) and females (macrogametocytes) are shown in the table on p. 189, and Figs. 44 and 45.

MOSQUITO CYCLE. When removed from the warm blood by being sucked up by a mosquito, or even if placed on a microscope slide, the microgametocytes undergo a striking development. The nucleus quickly divides, and within 10 or 15 minutes six to eight long flagella-like structures are extruded; the parasite is then known as a "flagellated body." This process of exflagellation is in reality the formation of microgametes. These slender structures break free and swim actively among the corpuscles ingested by the mosquito, in search of a macrogamete. The macrogametes meanwhile undergo little change except that the *falciparum* crescents become rounded (Figs. 46, 15, 16).

The result of the union of the filament from the flagellated body with the inactive female gamete is a "zygote." This new individual, the beginning of a new generation, grows, elongates, and becomes quite like a little worm (Fig. 46, 19, 20); it is 18 to 24 μ in length and 3 to 5 μ in width, and is called a vermicule or oökinete. It now penetrates the stomach wall of the mosquito, lodging itself under the outer limiting membrane. Here rapid growth takes place, and a cyst wall develops, formed partly by the parasite, and partly by the elastic membrane lining the mosquito's stomach. The oöcyst thus formed pro-

trudes like a little wart on the outer surface of the stomach wall (Fig. 48) and grows until it has a diameter of 50 to 60 μ .

Meanwhile its contents undergo important changes. The nucleus divides repeatedly, and a number of faintly outlined cells called sporoblasts are formed, varying in size and number (Fig. 46, 23). As further nuclear division occurs, dots of refractile chromatin arrange themselves around the periphery of each sporoblast. Granular streaks appear in

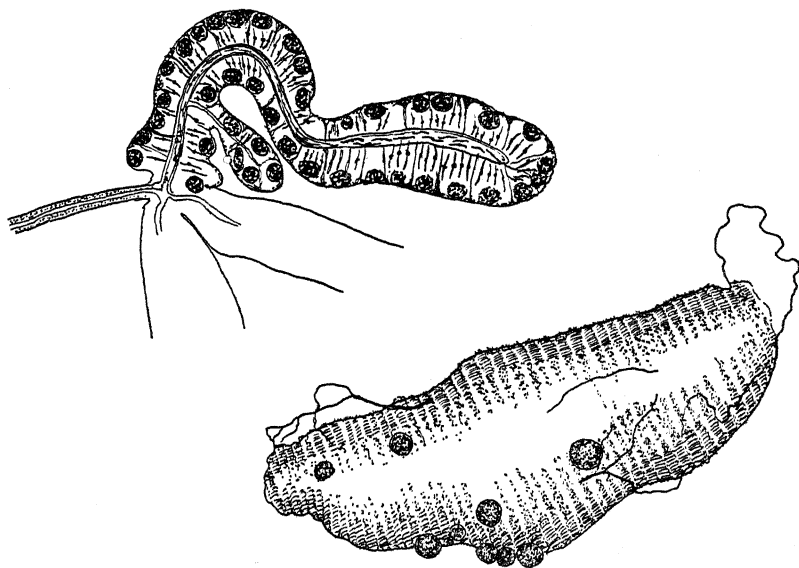


FIG. 48. Upper: One lobe of 3-lobed salivary gland of an infected mosquito, showing sporozoites in cells and lumen. Lower: Stomach of *Anopheles quadrimaculatus*, showing oöcysts of *Plasmodium vivax*.

the protoplasm, and slender spindle-shaped sporozoites develop, each with a chromatin dot as a nucleus. The sporoblasts, meanwhile, enlarge and coalesce, vacuoles form in them, and a sponge-like mesh is produced (Fig. 46, 24). Eventually the sporozoites, each about 15 μ in length, break loose from their moorings and form a tangled mass in the oöcyst, which is crammed with them to the bursting point (Fig. 46, 25). Such an oöcyst may contain more than 10,000 sporozoites, and there may be as many as 50 oöcysts on one mosquito's stomach. In about 10 days to 3 weeks, according to temperature, after the mosquito has sucked blood containing gametocytes, the oöcyst becomes mature and bursts, releasing the sporozoites into the body cavity of the mosquito. From here they make their way to the three-lobed salivary gland lying in the fore part of the thorax and connecting with the proboscis. They

assemble in the cells lining the salivary glands (Fig. 48); there may be up to 200,000 in one mosquito. The sporozoites now invade the lumen of the ducts and are discharged with the saliva when the mosquito bites. Many more may be discharged at one bite than at another, but it takes 20 bites or more to discharge them all.

James in 1926 reported one remarkable mosquito which was caught on August 5 and was finally dissected on November 16 of the same year, with active sporozoites still in its salivary glands. In the meantime it had spent a hectic life in incubators, refrigerators, hospitals, railway trains, etc., and had successfully infected more than forty general paralysis patients as a means of treatment. Humidity does not affect the cycle of development in the mosquito if the mosquito itself can survive.

Usually the number of oöcysts which develop on a mosquito's stomach is proportional to the number of gametocytes in the blood sucked, but only a small percentage actually develop. The number of sporozoites in the salivary glands may have little relation to the number of oöcysts; sometimes the development never goes beyond the oöcyst stage. The oöcysts of various species of malaria parasites are distinguishable by the number and character of the pigment granules, according to Shute and Maryon (1952).

The differences in the mosquito development of the different species are only minor. Infective gametocytes of *vivax* may appear in the blood of a patient within 4 days after the first appearance of the parasites. As few as 10 gametocytes per cubic millimeter of blood may be enough to infect *Anopheles quadrimaculatus*. Infective gametocytes of *falciparum* are not observed until 10 days after appearance of the parasites, and no infections of *A. quadrimaculatus* are successful with less than about 100 gametocytes per cubic millimeter. However, there is no close correlation between the number of gametocytes in the blood and infectiveness for mosquitoes; the gametocytes in some patients seem to be quite worthless, although the reason is unknown. Sometimes when bird malaria is inoculated into unfavorable hosts the gametocytes lack sexual potency although normal in appearance. The effect of drugs on viability of gametocytes is considered in the section on treatment, p. 207.

Temperature affects the time required for development in mosquitoes. At 85° to 90°F. both *falciparum* and *vivax* may form sporozoites in 7 or 8 days, though the mosquito mortality is high; 98°F. for even 4 hours prevents development entirely after an infective meal, and that temperature for 18 to 21 hours kills growing oöcysts. At 77°F. *vivax* oöcysts develop in 9 days, *falciparum* in 10 days, *ovale* in 15 days, and

malariae in 15 to 21 days. *Vivax* stands low temperatures better than *falciparum*; the former has its development stopped below 60°F., the latter below 66°F. Although development is stopped by cold weather, the parasites may remain alive and resume development later, but the minimum temperature at which microgametes are formed is said by Grassi to be 65°F., so no mosquito infections would be expected below that point.

The Disease. Although the course of a typical initial case of malaria, with its recurring chills and fever, is very easy for any physician to diagnose, even if he never saw one before, the symptoms may be profoundly modified by treatment, immunity, etc., particularly in old or repeated infections.

In some cases the gastro-intestinal tract is affected and symptoms resembling cholera or dysentery develop, either due to the malarial infection alone or to the lighting up of a chronic dysentery infection. In some the symptoms are suggestive of influenza or bronchopneumonia; in others, of dengue; in others, of encephalitis or meningitis. Sometimes the only symptoms are jaundice, anemia, albuminuria, malaise, or digestive disturbances. Any individual who has lived in a malarial locality and shows symptoms of a chronic infection not otherwise diagnosed should be suspected of malaria and his blood should be examined for it. Such blood examinations should be as routine as Wassermann tests or urinalysis.

In typical cases of primary *vivax* infections, after completion of one or two pre-erythrocytic cycles in the tissues, the parasites invade the blood stream about 7 to 14 days after infection, and are demonstrable in the blood a few days later. The time of appearance of blood parasites is usually a little shorter in *falciparum* infections and longer in *malariae* infections. In infections caused by temperate-zone strains of *P. vivax* this early invasion of the blood, resulting in an early primary attack, sometimes either fails to develop, or produces such mild attacks as to be unnoticed. Characteristic symptoms appear when the parasites have reached a concentration of about 200 per cubic millimeters of blood, or about one billion in the entire body.

The characteristic recurrent chills and fever of malaria are correlated with the liberation of successive broods of merozoites from disrupted blood corpuscles. As noted on p. 194, the intervals between sporulations of the parasites and consequent paroxysms is at first irregular, tending to be quotidian before it eventually assumes the typical 48- or 72-hour cycle. In relapses and in subsequent infections the appearance of the paroxysms on every second or third day may be apparent from the beginning.

Each attack begins with a shivering chill, sometimes accompanied by convulsions so severe that the teeth chatter, gooseflesh stands out, and the bed rattles. Yet the temperature will be found to be several degrees above normal and still going up. In the wake of the chill comes a burning and weakening fever, with violent headache and nausea and a temperature up to 106° or even higher. The fever stage in turn is followed by a period of sweating so profuse that the clothes or bedding may become wringing wet. The sweating gradually subsides, the temperature drops rapidly, often below normal, and after 6 to 10 hours the patient rests fairly easily until the next attack. The fact that the attacks most commonly occur between midnight and noon, instead of in the evening, is often useful in distinguishing malaria from other intermittent fevers.

In *P. vivax* infections the paroxysms of chills and fever continue every other day for 8 or 10 days to 2 weeks or more. Then they become less pronounced, the parasites become sparse, the patient feels well, and his temperature becomes normal. Sooner or later there are relapses, in which the intermittent chills and fever begin again. In temperate-zone strains of *P. vivax* (e.g., St. Elizabeth), after the primary attack (if any) has subsided, the exo-erythrocytic parasites usually remain quiescent for 6 to 14 months, commonly about 9 months. An interesting example of this occurred in a non-endemic area in California (Brunetti, 1954). A Korean veteran suffered a relapse of *vivax* malaria while camping near an encampment of Campfire Girls and was apparently responsible for 34 cases among the girls; 9 of these had incubation periods of 12 to 38 days, but 25 showed no symptoms until 7 to 10 months later.

When the relapses begin after the long latent period they occur repeatedly at intervals of a month or so. After these have subsided some strains (e.g., in Korea) apparently die out, but others may persist for years. The long latent period between primary and relapse attacks has been observed in strains of *P. vivax* from United States, Europe, Madagascar, and Korea. In at least some *vivax* strains that are of tropical origin, on the other hand, e.g., the "Chesson" strain from New Guinea, there is a series of short-period relapses, gradually spaced further apart and ending after about 18 months. The spacing and probability of relapses are, however, apparently influenced by dosage of sporozoites, acquisition of immunity, and administration of drugs (see Coatney and Cooper, 1948). It is commonly accepted that relapses after long periods may be brought on by such physiological shocks as exhaustion, childbirth, operations, alcoholic binges, etc., but there is a dearth of controlled evidence.

After repeated attacks the patient's vitality is lowered, he becomes anemic, his spleen enlarges, and he finally reaches a chronic run-down condition, at least when there is poor nutrition.

P. ovale infections are not prone to relapse and are more susceptible than any of the other species to drug treatment.

In *P. malariae* infections the paroxysms occur at 72-hour intervals, are milder and of shorter duration, recur more regularly, and the infections persist for a longer time. The milder nature of the disease often results in failure to seek treatment, and this, together with its long duration and tendency to relapse, is believed to explain the frequent kidney disease which is found in quartan cases. Lambers found nephritis in nearly 50 per cent of such cases in a hospital in Dutch Guiana as compared with 4 or 5 per cent in *vivax* and *falciparum* infections; one-sixth of all the nephritis cases were due to quartan malaria.

In *falciparum* malaria we have to deal with quite a different disease. In natives of hyperendemic localities, primary infections are seldom seen except in very young children but are common in visitors. The paroxysms of chills and fever are less well defined, last 12 or 14 to 36 hours, are severe in nature, and often occur daily, a fresh attack sometimes beginning before the previous one has entirely subsided. On days intervening between attacks the patient is sick and does not have a "well" day as in *vivax* infections. As already noted, the parasites frequently become excessively numerous and the spleen becomes very large. The temperature is likely to rise above 105°F., and is often accompanied by vomiting and delirium. The attacks usually last 8 or 10 days, and then the temperature slopes off. In just a few days, however, there is a second series of paroxysms, perhaps even more severe, and these recrudescences then continue in declining severity every 10 or 12 days for about 6 or 8 weeks, after which they become more irregular, although the blood continues to be infective. In the absence of reinfections the disease usually dies out completely in 6 to 8 months. In malarial countries in the tropics, however, no such course is seen, since reinfection is more or less continuous. Under these circumstances the infected persons become "carriers" harboring a few parasites, possibly too few to be found in blood smears, and showing few symptoms or none at all. In subtropical regions, on the other hand, as in southern United States and Italy, the infections die out in cold weather and fresh outbreaks occur every year.

A number of pernicious conditions may develop, usually in *falciparum* malaria. The tendency of corpuscles infected with *P. falciparum* to cling together results in clogging capillaries and preventing the proper flow of blood in vital organs. In the brain this, as well as a direct

toxic effect, leads to numerous symptoms, among them total loss of consciousness, or coma, and sometimes sudden death by a "stroke." This "cerebral malaria" causes a large fraction of malarial deaths. In some cases violent gastro-intestinal symptoms resembling cholera, typhoid, or dysentery develop, and in others, heart failure or pneumonia. *Falciparum* malaria is always an accompaniment of black-water fever, but its exact relation to that disease is still uncertain (see p. 209).

Prenatal infection is not infrequent, especially in *falciparum* malaria. Gastro-intestinal and pulmonary forms of malaria are especially common in infants.

Immunity. The nature of the acquired resistance to an existing malaria infection and immunity to superinfections has been extensively studied. From the very beginning of an infection there is considerable destruction of the parasites. Knowles pointed out that a single parasite producing twenty merozoites at each successive multiplication, if unchecked, would have increased in 20 days to the point where there would be about four parasites to every blood corpuscle, if the patient could live that long.

Much information, most of it probably applicable to human malaria, has been obtained about the development of immunity in malaria of birds and monkeys. Huff and his colleagues showed that in bird malaria immunity to blood forms does not protect against exo-erythrocytic forms, and they think it possible that two different antibodies may be involved. In human malaria where the e.e. forms are far less abundant than in some bird species, it is doubtful that complete immunity to e.e. forms ever develops.

The mechanism on which the blood immunity depends has been demonstrated by Taliaferro and his colleagues to be mainly phagocytosis by cells of the reticulo-endothelial system, particularly in the spleen, liver, and bone marrow. The phagocytosis begins probably at once, and consists of the engulfing and destruction of the entire parasitized blood corpuscles and not merely the free merozoites. This destruction of invaded corpuscles is believed to be an important factor in malarial anemia. As the disease progresses the activity of these voracious cells is gradually increased, and they begin multiplying in number until a climax is reached when the rate of destruction of parasites greatly exceeds their production. At this time the liver and spleen are enlarged and show great activity of the phagocytic cells in them. There is also a marked increase in lymphoid tissue to build a mesenchymal reserve for the rapid production and mobilization of more macrophages.

This condition gradually declines during the latent period, but rapid mobilization against fresh invaders of the same species may occur for years, especially if the infection has not entirely died out. The immunity is, however, highly specific, and not only fails to protect against attack by other species but sometimes even by other strains of the same species. In well-nourished and healthy individuals, as long as the parasites persist in the body in an exo-erythrocytic reservoir, as in *vivax* and *malariae* infections, or are constantly being reinoculated, as in *falciparum* infections in the tropics, the immunity, once developed, is restimulated as soon as it begins to fail because of scarcity or lack of parasites, and no clinical relapses can occur. Only unhealthy individuals, who are unable to provide for rapid formation of antibodies or phagocytes in response to a renewed stimulus, suffer a relapse before the body reacts.

The presumed absence of an exo-erythrocytic reservoir in *falciparum* infections, and the wiping out of the blood infection in 6 or 8 months, before a high enough degree of immunity is built up to persist very long, results in the tendency of this infection to break into epidemics in areas where conditions are not suitable for continued reinfection, e.g., on the fringes of the tropics (see p. 203). Under such conditions it may be dangerous to control malaria partially in a hyperendemic area or to create a non-malarial oasis in its midst unless facilities for prompt treatment of cases are available.

Infants in hyperendemic areas do not suffer as much as is sometimes thought from malaria infections since, as in the case of a number of other diseases, they are passively protected by the mother's antibodies until they begin to develop some of their own.

Negroes have a higher degree of tolerance to malaria parasites than do Whites. Many are refractory to infection even with exotic strains to which they could not have developed specific immunity. Watson and Rice in a study in the Tennessee Valley in 1946, found that although the parasitemia rate in Negroes was five times that in Whites, the Whites experienced about ten times as many reported cases of malaria and over fifteen times as many sick days.

Epidemiology. As a result of the work of Ross and Grassi, which set such an important milestone in the progress of preventive medicine, malaria is now known to be transmitted naturally, except in some pre-natal infections, only by the bites of certain species of mosquitoes, all belonging to the genus *Anopheles*.

The only important exception is in the case of heroin addicts, who frequently pass infections around by means of hypodermic needles.

More than a hundred species of *Anopheles* have been described, but less than two dozen species are of any real importance in the transmission of malaria, except perhaps in local areas. This matter is discussed in the chapter on mosquitoes (p. 712). As shown there, some species are eliminated because they do not readily nurse the malaria parasites through their sporogonic cycle; some are eliminated because of their habits; and others are of no importance on account of their rarity. Local conditions may influence the importance of particular species of mosquitoes in transmitting malaria, and therefore local epidemiological surveys to determine the prevalent transmitters are important. Since the different species vary greatly in their breeding habits, control measures must depend on the habits of the particular species involved.

Malaria does not become endemic wherever suitable *Anopheles* mosquitoes occur. A small deviation above or below the critical point may mean the difference between ultimate extermination and permanent establishment. MacDonald (1952) speaks of a "critical density," meaning the average number of *Anopheles* bites per person per night below which there would be progressive reduction of the disease until it became extinct, as has now happened in the United States. The critical density is determined by a number of factors: number of mosquitoes, fondness for human blood, life expectancy of the mosquitoes, frequency of feeding, extent of development of parasites to the sporozoite stage, etc. For example, where malaria is transmitted by such mosquitoes as *A. gambiae*, *A. funestus*, and *A. minimus*, the critical density is low (0.029 for *A. gambiae*) and we have stable malaria; where transmitted by such species as *quadrimaculatus* and *albimanus*, which have high critical densities, malaria is unstable, i.e., easily influenced by environmental and climatic changes.

Food preferences of various different species or varieties of *Anopheles* are of prime importance. The presence of abundant *Anopheles* in certain localities in Europe without accompanying malaria when neighboring localities with fewer *Anopheles* might be highly malarious was a mystery until it was found that the European *A. maculipennis* really consists of several distinct races, some of which are "zoophilic" and only exceptionally bite man, whereas others show no discrimination against human blood (see pp. 712-713). Tendency to enter houses, and particularly to rest in them after feeding, is of great importance in connection with the effectiveness of DDT residual spraying; the latter causes great reduction of malaria where such species as *quadrimaculatus* and *darlingi* are the transmitters, but has little effect where *aquasalis* or *bellator* are principally involved.

Climate is a factor, for it may lower the life expectancy of most of the mosquitoes to a point where there may not even be time for the sporogonic cycle of the malaria parasites to be completed. In Punjab, for instance, there is little transmission, even with abundant potential transmitters, when the season is hot and dry.

The species or strains of malaria parasites are also important. Some mosquitoes become infected much more easily with some species or strains of parasites than others. The susceptibility of *A. quadrimaculatus* to *P. falciparum* as compared with *A. crucians* is in the ratio of 64 to 15. *A. maculipennis atroparvus* in England proved refractory to Indian and African strains of *falciparum*, but not to European ones. An infected *A. quadrimaculatus* usually transmits *P. falciparum* by a single bite, whereas it often requires several bites to transmit *vivax*, but this mosquito seems to be susceptible to most if not all strains of both *vivax* and *falciparum*. *A. albimanus* from Cuba or Panama, though highly susceptible to malaria strains from its own region, is refractory to Florida strains. Huff, working with *Culex* vectors of bird malaria, found that refractoriness of mosquitoes to malarial infection is hereditarily transmitted.

As noted on p. 201, epidemics of *vivax* malaria rarely occur since the disease often continues to exist in the host for several years, keeping up immunity by occasional relapses. Only if a new strain of *P. vivax* were introduced from foreign parts could an epidemic occur. In hyperendemic tropical regions there are no *falciparum* epidemics either, the reason being constant reinfection.

In subtropical areas where climatic conditions are such as to cause marked seasonal reduction in anopheline density, true epidemics of *falciparum*, and to a less extent of the other species, may occur; their violence is largely dependent upon the interval between seasons of highly favorable conditions for infection. An epidemic may occur of such extraordinary severity as to involve almost the entire population and to cause a mortality of several hundreds per thousand. Such devastating epidemics are nearly always of the *falciparum* type.

Local epidemics may also arise from the bringing in of a new strain of parasite, from the introduction of a new species of *Anopheles*, e.g., *A. gambiae* into Brazil and during World War II into Egypt, or from the development of more favorable conditions for the breeding of dangerous species of *Anopheles*. In parts of Europe inhabited by zoophilic strains of *maculipennis*, malaria disappears as animal husbandry develops. In Java improvement and reconstruction of houses for protection against plague has led to a serious increase in malaria; this is apparently due to a combination of several factors, such as tile

roofs, borrow pits for building material, and importation of new parasite strains with laborers.

Diagnosis. In acute cases of malaria the clinical symptoms are usually sufficient for a diagnosis. In more chronic cases a combination of anemia and enlarged spleen, where kala-azar and certain less common conditions can be ruled out, almost unmistakably advertises malaria infection. Nevertheless all diagnosis should be confirmed by blood examination whenever possible. If not possible, failure of a test course of an anti-malarial drug to relieve the symptoms indicates that the fever is not due to malaria.

Accurate diagnosis is made by examinations of blood smears stained by a Romanowsky stain, preferably Giemsa's. In thin smears, made by spreading a film on a slide by drawing a drop across it in the acute angle behind the line of contact of the film slide and the spreading slide, the infected corpuscles are spread in a single layer, and the parasites are stained in their natural positions in the corpuscles. Characters which differentiate the species and stages are easily recognizable in such films. Thick smears, however, are far more valuable for detection of cases in which the parasites are sparse, though the identification is more difficult. These smears are made by thoroughly drying thick drops, dehemoglobinizing before or during staining, and then examining for the more concentrated parasites free from the corpuscles. An injection of adrenalin a few minutes before taking the blood for a smear is helpful in finding parasites when they are sparse.

The degree of malariousness of a district can be determined fairly accurately by finding the percentage of children between about 2 and 10 years of age who have enlarged spleens. The "spleen rate" in adults is of little value in highly malarial places because of a reduction in spleen enlargement with continued immunity; it is of use only as an indication of the number of active cases. Any spleen that can be felt below the last rib when a child is lying down may be classed as enlarged and is usually indicative of malaria; in extreme cases the spleen may reach the pubis.

Serological tests for malaria have been recommended but are not generally considered reliable enough to replace examination for parasites.

Treatment. The treatment of malaria has come a long way from the time a Countess Chinchona, returning to Europe from Peru in 1640, introduced a native Indian remedy, "fever bark," containing quinine and allied alkaloids. These alkaloids, especially quinine, remained the standard treatment for malaria for 300 years. Now, however, it is still used only by physicians who haven't kept up with the times.

Since quinine had little effect on gametocytes, especially of *P. falciparum*, and did not prevent relapses of *vivax* and quartan malaria, search was made for better drugs. During World War II this search was so intensified that more research was directed toward finding better antimalarial drugs than toward any other project except the atom bomb. Prior to the war two drugs had been found that were helpful; one, Plasmochin (Pamaquin), was found in 1926 to kill the gametocytes that quinine didn't, and to be helpful in preventing relapses, but it was too toxic to use on a large scale; the other, atebirin (Quinacrine, Mepacrine), was a substitute for quinine which was, as a rule, better tolerated and more effective, its chief disadvantage being that it temporarily turns the skin a bilious saffron color. It was, however, an incalculable boon during World War II; then the quinine supply was cut off by the Japanese at a time when it was needed more than ever before.

Meanwhile, the discovery of the exo-erythrocytic forms of *P. gallinaceum* and evidence of their occurrence in human malaria, together with the fact that drugs which affect the schizonts in the blood have little or no effect on the e.e. forms, made it evident why these drugs, although suppressing *vivax* and quartan malaria and rapidly controlling the symptoms by killing the blood parasites, failed to bring about complete cures and therefore to prevent relapses. From the fact that *falciparum* malaria is not only suppressed but also cured by the "schizonticides," it has been deduced that in this species the exo-erythrocytic schizogony does not continue long, if at all, after the pre-erythrocytic development, and therefore when the blood parasites are destroyed by drugs, or by immune reaction, the infection dies.

The search for anti-malarial drugs during and after World War II therefore resolved itself into: (1) Finding better schizonticides to destroy the blood parasites and therefore, in *vivax* and quartan malaria, to cure clinical symptoms in developed cases and prevent development of symptoms from new cases as long as the drug is being administered, i.e., act as a suppressant; and in *falciparum* malaria, radically to cure developed cases and prevent new infections from ever producing clinical symptoms even after discontinuance of the drug, i.e., act as a causal prophylactic. (2) Finding drugs which would destroy the e.e. forms of the parasite in the sporozoite, pre-erythrocytic or later e.e. stages, and, therefore, act as a causal prophylactic for all forms of malaria, and radically cure all forms.

Great progress has been made in both quests. Two effective schizonticides, Chloroquine and some related 4-aminoquinolines and Paludrine, were discovered during the war. In the postwar years some 8-amino-

quinolines, of which Primaquine is best, were found which are very effective against the tissue parasites, as well as another drug, Daraprim, which has astonishing suppressive activity.

Chloroquin (Resochin, Nivaquine B) and some related drugs (Camoquin, Sontochin, etc.) suppress *vivax* malaria and protect against *falciparum* infections in a single oral dose of 0.3 gram of the base once a week. Even for treatment of clinical cases a single oral dose of 0.8 to 1 gram or less of the base is usually adequate and can be used in mass treatments. The temperature becomes normal within 18 hours, and the parasites disappear within 25 hours. When feasible, a 3-day regimen is preferred—3 doses of 0.3 gram first day, then a single 0.3-gram dose for two more days.

Paludrine (chlorguanide) is also good, but it is slower in action, is less effective against some strains of malaria, and tends to produce drug-resistant strains. Its advantages are cheapness, lack of toxicity, and activity against gametocytes; the latter are slow in disappearing but are rendered non-infective for mosquitoes in a day or two.

Although the tissue forms of malaria parasites are affected to some degree by sulfonamides, some antibiotics, and a few other drugs, only certain 8-aminoquinolines and a pyrimidine (Daraprim) have been found sufficiently active to warrant extensive use as radical cures and causal prophylactics of the relapsing forms of malaria (*vivax* and *malariae*). Unfortunately, the 8-aminoquinolines have rather narrow margins of safety between the effective therapeutic doses and toxic ones; they cause acute hemolytic anemia in some individuals, due to an intrinsic susceptibility of their older corpuscles. Plasmochin, the first one used, had a very narrow margin of safety. Then Pentaquine and Isopentaquine were tried, each less toxic than the other, and effective in smaller doses, but still not safe enough. Then about 1950 another drug, Primaquine, was found not only to be superior to the other drugs, but also to be very well tolerated except in a few cases. Its pharmacological properties and effectiveness against malaria were thoroughly studied by Schmidt and his colleagues on *P. cynomolgi* infections in monkeys, and it was then tested on a large number of American troops returning from Korea. A dose of 15 mg. of the base daily for 14 days, plus 1.5 grams Chloroquine in divided doses in 3 days (see above), caused complete cures of *vivax* malaria, with no relapses. Larger doses sometimes produce toxic symptoms. Even in Negroes, who develop anemia more readily than Whites, double this dose (30 mg.) daily for 14 days produced mild anemia in only 17 of 105, and severe anemia, making it necessary to discontinue treatment, in only 5 Negroes.

Daraprim, a different type of anti-malarial drug, is the most potent one yet discovered, and is unique in being highly effective against *both* blood and tissue forms. Single doses of 25 mg. cause schizonts of *vivax* and *malariae* to disappear, and prevent them from reappearing for a month; and even doses as small as 5 mg. will temporarily clear the parasites. Less than 1 mg. a week suppressed them. In acute attacks, however, Daraprim does not clear parasites or fever as rapidly or effectively as Chloroquine. Early indications were that the drug also destroyed the e.e. forms and was therefore a true causal prophylactic and means of cure; this proved not always to be true, even after 17 weekly doses of 25 mg., but there are long delays after cessation of treatment before relapses occur. In a dose of 25 mg. weekly, or at even longer intervals, Daraprim is a completely reliable suppressant of all forms of malaria, and at that dosage is non-toxic. Although it does not kill gametocytes, it prevents their normal development in mosquitoes, thus preventing transmission. Its slow action in active cases, failure to radically cure *vivax* infections, and tendency of parasites to develop resistance to it are disadvantages; its greatest usefulness is for routine suppression. In some African villages, weekly doses of 25 mg. for 15 weeks virtually eliminated malaria parasites from mosquitoes as well as from the blood of the human population. It was suggested that an annual course of treatment early in the rainy season might help to eradicate malaria over wide areas.

In addition to treatment with specific drugs, there is no doubt, as already pointed out, that nutrition is an important factor in determining the severity of malaria in a community. Of particular interest is the observation that a pure milk diet suppresses *P. berghei* in rats and mice; evidently some factor necessary for the parasites is lacking, since milk *ad lib.* with a normal diet is not suppressive. That milk may have a similar effect on human malaria parasites is suggested by the rarity of malaria in infants under 3 months of age, but some experiments with adults failed to support this view.

Prevention. Although the control of malaria has been relatively simple in principle ever since the discovery by Ross and Grassi of its means of transmission, in practice it has not been easy. It requires community rather than individual effort. Even with our relatively new tools—DDT and suppressive drugs—Ross' statement made many years ago is still true: "It [malaria] is essentially a political disease—one which affects the welfare of whole countries; and the prevention of it should therefore be an important branch of public administration. For the state as for the individual health is the first postulate of prosperity. And prosperity should be the first object of scientific govern-

ment." Often in the past, however, private industrial organizations have been more active in malaria control than have the governments.

A brilliant example of malaria control was the elimination, in 1939-1940, of the disease in northeastern Brazil by the complete eradication of *Anopheles gambiae*, made possible by a cooperative project financed by the Brazilian government and the Rockefeller Foundation. Introduced from Africa to Natal, Brazil, in 1930, *A. gambiae* spread hundreds of miles to northeastern Brazil and created a malaria epidemic that has probably never been equaled in intensity. The need for constant guard against reintroducing of this species is evident, however, from the fact that in 1943 living specimens were found several times in planes arriving from Africa and once in homes near the Natal airport.

With the advent of residual spraying with DDT and related chemicals, and to a lesser extent their use as mosquito larvicides, together with easy and safe prophylactic and suppressive treatment, previously undreamed of progress has been made in the control, or even complete elimination, of malaria, even from large areas in some of the most malaria-ridden countries in the world. The elimination from the United States and the reduction or local eradication in a number of other parts of the world have already been mentioned (p. 186). The major malarial control programs of recent years include Transvaal, Madagascar, and South Rhodesia in Africa; Mauritius in the Indian Ocean; Ceylon, parts of India and Pakistan, Afghanistan, Indonesia and Indo-China in Asia; Italy, Sardinia, Greece, Portugal, and Yugoslavia in Europe; and United States, Mexico, Costa Rica, and most of the countries in South America. Pampana (1951) estimated that the residual spray program alone is eliminating malaria which affected nearly half a billion people. The great value of residual spraying with DDT or related compounds (see p. 515) is that a high percentage of the mosquitoes which bite malarial patients in or around houses, privies, etc., by resting on the sprayed walls after a feed, will die before they can transmit the disease.

The prospect for control of malaria is not as good in places where the principal vectors do not enter houses, or enter only to bite and run (see p. 736). Here it will be necessary to destroy the breeding places or kill the larvae of the vectors, or use suppressive drugs (Daraprim or chloroquine), a procedure which might lead to ultimate eradication.

The control of malaria by anti-mosquito methods is not a problem of general mosquito control, or even *Anopheles* control, but *species* control directed against one or two important local vectors in the particular locality. It is of paramount importance to identify the principal malaria

carriers of a region, to study their habits, and then to institute measures directed specifically against these. There are less than two dozen dangerous malaria-carrying species of *Anopheles* in the whole world, but sometimes the habits of individual species vary from place to place, so local studies of them are required.

Except in the case of imperfectly adjusted immigrant species of mosquitoes (e.g. *Anopheles gambiae* in Brazil and Egypt) or under special conditions, such as *A. pseudopunctipennis* in the separated mountain valleys of Chile, complete elimination of malaria-carrying species of mosquitoes is difficult, expensive, and unnecessary. Reducing them to the critical density (see p. 202) is enough. After complete stoppage of malaria transmission over a large area for several years, control operations may be discontinued.

An important fact that is often overlooked is that much malaria is man-made, e.g., by engineers who carelessly leave borrow pits, dam up streams, etc., by irrigation, flooding, impounding, etc., or even, as in Trinidad, by planting forest shade trees that harbor aerial plants (bromeliads) in which *A. bellator* breeds.

During military operations bomb craters, shell holes, foxholes, ditches, vehicle ruts, etc., made many an *Anopheles* happy, for under natural conditions even mosquitoes are often troubled by what corresponds to a housing shortage. Man is an occasionally rational being who in the past has probably done as much to help malaria as he has done to eradicate it.

Although there will be some areas in which malaria will continue to thrive for a while, or perhaps even increase, Soper's estimate that 90 per cent of the malaria in the world can be wiped out by 1960 is not a pipe dream.

Blackwater Fever

In many parts of the world where severe malignant tertian malaria is present, but not in all, a disease occurs which is known as blackwater fever, about the real nature of which there has been much argument but little definite knowledge. It is a scourge in many parts of Africa and in some parts of India, Malaya, and the East Indies, and formerly in the southeastern United States. The disease is characterized by a fever accompanied by an intense jaundice and a tremendous destruction of red corpuscles and excretion of hemoglobin in the urine. In severe cases 60 to 80 per cent of the red blood corpuscles may be destroyed within 24 hours. The disease is usually accompanied by a contraction of the spleen. Severe attacks are usually fatal; cases that recover are prone to subsequent attacks if they remain in an endemic area. Often

a blackwater fever attack wipes out the malarial infection. The disease is suggestive of the course of *P. knowlesi* infections in rhesus monkeys.

As yet the reason for the common occurrence of blackwater fever in *falciparum* malaria cases in some areas but not others is unknown; a review of current theories was made by Macgrath (1946). To the writer the evidence strongly suggests some antigen-antibody mechanism which reacts against the corpuscles and hemolyzes them, possibly involving something comparable to the Rh factor. Debility, attacks of malaria in adults who have developed no immunity, malnutrition, exhaustion, and exposure to cold seem to be predisposing factors.

Treatment with quinine or the 8-aminoquinolines is contra-indicated, but atebirin or chloroquine can be given safely. Patients should stay in bed, keep the skin warm and carefully protected from drafts, and drink plenty of warm, salty, alkaline fluids. About half the deaths are due to kidney failure. Complete quiet, diuretics, and a milk diet are recommended, with intravenous saline or glucose injections in some cases, as well as blood transfusions. Enough alkali should be given to make the urine alkaline. Some authors have found injections of liver extract to be of great benefit if given along with atebirin.

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BLACKWATER FEVER

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Other Sporozoa, and
Arthropod-Borne Microorganisms
Other than Protozoa

SPOROZOA OTHER THAN MALARIA

Haemosporidia

As noted on p. 181, the subclass Haemosporidia contains (1) the order Plasmodiida, considered in the last chapter; (2) the order Babesiida, containing the single family Babesiidae; and (3) some other parasites of uncertain affinities, e.g., *Toxoplasma*. These as well as other Sporozoa, of interest as parasites of man or domestic animals, will be considered in the present chapter. A brief bird's-eye view will also be given of the characteristics and relationships of arthropod-borne microorganisms other than Protozoa—rickettsias, viruses, and bacteria.

BABESIIDAE

The general characteristics of this group of parasites were given on p. 181. The life cycles are rather imperfectly known, even in the most important species, and most of them are entirely unknown. Eight or ten genera have been described. Members of the genera *Babesia* (= *Piroplasma*) and *Theileria* cause important and highly destructive diseases of all the large herbivorous animals and also of dogs, and species of *Aegyptianella* are injurious to poultry. All species of Babesiidae as far as is known are transmitted by ticks. In the genus *Babesia* the parasites are known to multiply only in the red blood corpuscles; they are usually pear-shaped, and grouped in twos or fours (Fig. 49, A-G). In the genus *Theileria* the organisms are smaller, of variable shape, sometimes showing schizogony, and with no tendency to be grouped in pairs (Fig. 49, H-M). Schizogony occurs in cells of the lymphatic system, although one recently described from the duiker antelope, *Cytauxzoön sylvicaprae*, undergoes schizogony in histiocytes, more like the Plasmodiidae.

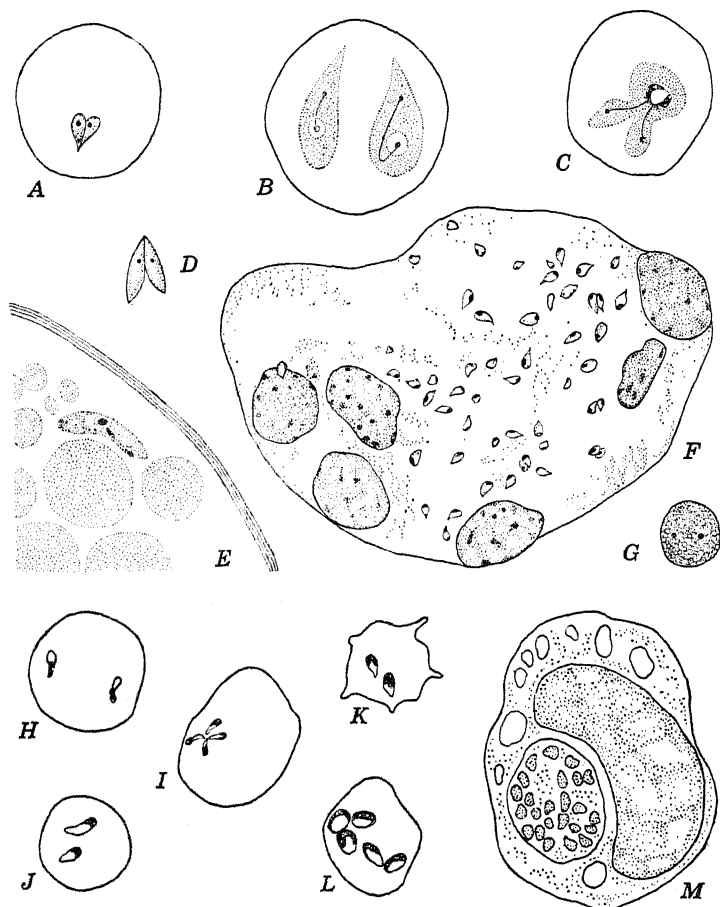


FIG. 49. A-G, *Babesia bigemina*; A-C, in cattle; D-G, in tick. A, trophozoite in red cell of cattle, showing binary fission; B, large pyriform pairs in red cell; C, division stage in red cell; D, associated isogametes in gut of tick; E, ookinete in section of ovum of tick; F, sporozoites in a single focal plane of salivary anlage of tick; G, late stage of syngamy of isogametes. (Adapted from Dennis, *Univ. Calif. Publ. Zool.*, 33, 1930; 36, 1932.)

H-M, *Theileria*; H-J, *T. mutans* in cattle blood; K-L, *T. parva* in cattle blood; M, leucocyte containing a schizont. (Adapted from Brumpt, *Bull. Soc. Path. Exot.*, 13, 1920, and *Ann. Parasitol.*, 1, 1923; and 2, 1924.)

Although about 20 species of *Babesia* have been named, many of these are probably not valid species, and only a few are important parasites of domestic animals. These include 3 species in cattle (*bigemina*, cosmopolitan; *argentina*, in South America; and *bovis*, in Europe); 2 species in sheep and goats (*ovis* and *motasi*, both in Europe and Africa); 2 species in pigs (*trautmanni* in Eastern Europe and Africa; *perroncitoi*

in Sardinia); 1 in horses (*caballi*, around Mediterranean and in Central America); and 2 in dogs (*canis*, in Europe, Asia, and Africa; *gibsoni* in Asia and Africa). There are also species of a related genus, *Nuttallia*, somewhat intermediate between *Babesia* and *Theileria*, which occur in horses and elephants in the Old World. It is obvious that most of the Babesiidae are limited to the Old World, but one species, *Babesia bigemina*, has a world-wide distribution in cattle.

The diseases caused by *Babesia*, often called piroplasmosis from the name *Piroplasma*, long used instead of *Babesia*, are characterized by destruction of red blood corpuscles and elimination of hemoglobin with the urine, hence the name "redwater fever." They produce fever, anemia, jaundice, and injury to the liver and kidneys. *B. bigemina* (Fig. 49, A-G) is the cause of Texas fever or redwater fever in cattle, of world-wide distribution. The disease is transmitted by ticks of the genus *Boöphilus* (see p. 562) in which the parasites, after fertilization in the hind gut, invade the reproductive organs. They become enclosed with the eggs and subsequently undergo extensive multiplication and migration to all the tissues of the developing tick embryo. Some of the parasites enter the salivary glands and can then be transmitted by the seed ticks when they feed (Dennis, 1932). The adult ticks do not transmit the infection. The developmental cycle of *Babesia* in the vertebrate host is not fully known; the only forms known are small oval or pear-shaped bodies which bud to produce clusters of two, or in some species four, parasites (Fig. 49, A-C). Some writers, however, have described what they interpret as schizogony in red cells. By quarantine and anti-tick methods this one-time scourge of cattle has been completely eliminated in the United States.

The genus *Theileria* (Fig. 49, H-M) contains about a half-dozen species which are very difficult to distinguish from one another; possibly they are only strains of one species. They are parasites of cattle, sheep, and goats (occasionally camels) in the Old World, except one species, separated into a separate genus *Rangelia*, which causes a form of redwater fever in dogs in Brazil. The true *Theileria* do not cause anemia, jaundice, and hemoglobinuria as do the species of *Babesia*, but they do cause fever.

In the deadly East Coast fever of cattle in Africa, caused by *T. parva*, after about 15 days of fever the animals seem to be convalescing and then often suddenly fall over and die, apparently from edema of the lungs. In grown animals the mortality may be 95 per cent. A closely related form, *T. mutans*, causes a practically symptomless infection of cattle over most of the Old World, and similar forms with varying degrees of pathogenicity attack sheep, goats, and camels.

The cycle of development of these parasites in the tick hosts has been worked out for only one species, *T. dispar* (= *T. annulata*), by Sargent et al. in 1936.

TOXOPLASMA

This organism is still one of the least understood of the parasites of man and domestic animals, although it is extremely common and under some circumstances very dangerous. As yet its taxonomic relationships are so little known that it is even suspected of being a fungus instead of a protozoan, and one man has argued for inclusion in the Trypanosomidae.

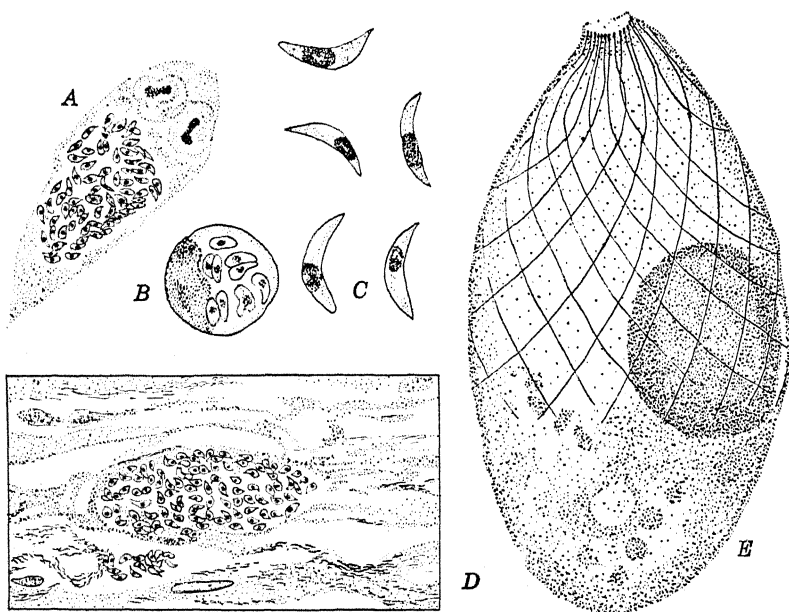


FIG. 50. *Toxoplasma gondii*. A, in liver cell of chick embryo in tissue culture; B and C, from peritoneal exudate of mouse, in cell and free; D, from heart muscle of dog; E, as seen by electron microscope. (A-D after Jacobs, *Am. J. Trop. Med. Hyg.*, 2, 1953; E after Bringmann and Holz, *Ztsch. Tropenmed. Parasitol.*, 5, 1954.)

The parasites (Fig. 50) are crescent-shaped or oval, 6 to 12 μ long, with a discrete central nucleus; they usually occur in pairs or groups of pairs and apparently multiply by binary fission. By electromicrography Bringman and Holz demonstrated an organelle at the anterior pole which may be a cell mouth or a hold-fast, and also fibrils extending over the anterior two-thirds of the body (Fig. 50E); these may

account for the active movement of the organism and its ability to penetrate cells. Similar fibrils occur in malarial sporozoites.

The parasites are found free in the blood stream or in tissues, or inside cells of many different types, particularly those of the reticulo-endothelial system, white blood cells, and epithelial cells. After experimental inoculations in laboratory animals the organisms appear free in the blood plasma and in various organs within 4 hours; they subsequently disappear from the blood, but in rats they are irregularly demonstrable in the liver, lungs, spleen, etc., for several weeks and are uniformly present in the brain for at least 2 years. Here, and sometimes in other parts of the body, in chronic symptomless cases they occur in large intracellular "pseudocysts" containing up to 50 or more organisms, apparently in an inactive resting state, since they cause no inflammatory reaction as do the free forms. It is believed that it is due to rupture of these pseudocysts, from unknown causes, that the infection sometimes flares up again in chronic cases.

As far as known there is only one species of *Toxoplasma*, *T. gondii*, which shows almost no choosiness about its hosts, apparently being able to infect all kinds of birds and mammals. As indicated by antibody tests, and in many cases by transmission to laboratory animals as well, this parasite has been reported to occur in 59 per cent of dogs, 34 per cent of cats, 48 per cent of goats, 30 per cent of pigs, 3 to over 20 per cent of rats, and 10 to 12 per cent of pigeons. In man the incidence of significantly positive antibody tests ranges from 0 per cent in eskimos to 68 per cent in Tahiti; in American cities the incidence ranges from 17 to 35 per cent. It will be observed that man's closest animal friends, dogs and cats, must constitute important reservoirs of the disease, and that rats, in addition to their long-known relation to plague and typhus, are important reservoirs of this disease as well; infective *Toxoplasma* was demonstrated in the brains of 14 of 160 wild rats in Savannah, Georgia, and in over 3 per cent in Memphis, Tennessee.

Nothing is known about the usual method of transmission, but pre-natal infections occur both in man and animals, and animals can be infected by eating infected flesh or feces. There is no evidence of seasonal infections, and person-to-person transmission seems rare. There is a high incidence of antibodies in rabbit handlers. Blood-sucking arthropods may play a part; fleas after feeding on infected animals are infective when eaten but not by bite.

In animals, toxoplasmosis may produce anything from rapidly fatal infections to inapparent ones. Mice, rabbits, and birds often suffer severely, but rats usually have mild and transient infections. In man,

the symptoms as a rule become less and less pronounced with advancing age. After the maturation of the defense mechanism (see p. 21) of human hosts, the parasites are usually got under control before they do serious damage. Only six fatal cases have been reported in human adults. Adults only rarely show symptoms, and children only mild ones, often only eye disturbances (chorioretinitis); but infants infected before birth usually die with severe infections which affect the brain and eyes particularly, these often being almost completely destroyed. In congenital cases there is almost always severe eye injury (chorioretinitis), hydrocephaly or microcephaly in two-thirds, and severe mental and nervous disturbances and convulsions in nearly all of them.

Undoubtedly, as in animals, these prenatal human infections are at first generalized, but as the mother develops antibodies and shares them with the fetus, the parasites are inhibited in the visceral organs but continue their devastating activity in the brain. As Frenkel and Friedlander (1951) point out, this "blood-brain barrier," as it is called, effective in all infectious diseases that penetrate into the central nervous system, is probably related to the fact that there is only about 0.3 to 0.5 per cent as much protein in the cerebrospinal fluid as in the blood, and a correspondingly small amount of antibody content. Hence parasites are able to persist in the central nervous system long after antibody reaction has made it too "hot" for them in other parts of the body.

Evidence indicates that infections in newborn babies result from prenatal infection from mothers that acquire infections, usually symptomless, during pregnancy, *not* to old chronic infections. Even if a baby survives it is often so severely damaged that it can lead only a vegetative existence. Children sometimes have transitory attacks of chorioretinitis due either to new infections or to relapses from the rupture of pseudocysts in the brain.

Aside from the finding of parasites by smears or animal inoculation, diagnosis of present or past infections may be made by several immunological tests. One is intradermal inoculation of an extract of the parasites called toxoplasmin; it is not very reliable. Another is complement fixation, but this is slow in development, and fades quickly. Most valuable is a "dye test" discovered by Sabin and Feldman (1948). When living parasites in mouse peritoneal fluid are placed in serum containing antibodies against *Toxoplasma*, along with a methylene blue dye and some normal human serum (preserved by freezing) to serve as "activator," the parasites lose their affinity for the dye, whereas in normal serum containing no antibodies they round up and have both the nucleus and cytoplasm stained. Sarcosporidia, more easily obtainable, can be substituted for *Toxoplasma* in this test. In serum dilutions

of 1 : 16 or greater this dye test appears to be a reliable index to present or past infection; it remains positive for as long as 25 years, although the titer gradually drops. This test becomes positive early in an infection, usually during the second week, quickly rises to a titer of 1 : 1000 or more, and then remains high for a year or more. A rising titer by either the dye test or complement fixation indicates an existing or very recent infection, but a single test may only mean past infection.

A combination of Daraprim (see p. 207) and sulfonamides shows promise in treatment, but, in rats at least, the parasites are less easily eliminated after 3 or 4 months, when "pseudocysts" presumably have formed. Antibiotics are useless.

Hepatozoön and Hemogregarines

These parasites, although classified in the subclass Coccidiida, resemble the Haemosporidia in requiring an intermediate host. The forms found in cold-blooded animals may belong to either of two genera: (1) *Haemogregarina*, in which the schizogonic cycle and the gametocytes (Fig. 43L) may both occur in blood corpuscles, and oöcysts containing free sporozoites develop in leeches; or (2) *Karyolysus*, in which schizogony occurs in endothelial cells, producing merozoites which enter red corpuscles and become gametocytes, the sporogonic cycle occurring in mites. The hemogregarines of birds and mammals are placed in the genus *Hepatozoön*; schizogony occurs in the reticulo-endothelial cells of liver, spleen, or bone marrow, and the gametocytes (Fig. 43K) develop in circulating mononuclear leucocytes. The sporogonic cycle of *Hepatozoön muris* of rats occurs in dermanyssid mites (see p. 536) of the genus *Laelaps*, whereas that of *H. canis* of dogs occurs in ixodid ticks. In these intermediate hosts there develop large coccidium-like oöcysts containing numerous sporocysts, each with about sixteen sporozoites. The resemblance to coccidians is further indicated by the fact that the sporocysts cause infection only via the alimentary canal, when swallowed with the mites or ticks in which they develop. *H. canis* causes a serious and sometimes fatal illness in dogs in India and Africa.

The gametocytes of hemogregarines in red cells are distinguishable from those of *Haemoproteus* by the lack of pigment.

Coccidia

General Account. Although negligible as human parasites, Coccidia cause a greater economic loss among domestic and game animals in temperate climates than any other group of Protozoa. They are of major importance to poultry raisers and produce serious disease in rabbits and cattle. Horses, sheep, goats, pigs, dogs, cats, guinea pigs,

ducks, geese, pigeons, and even canaries frequently suffer from their attacks. For relationships of the Coccidia to other Sporozoa, see pp. 180-181.

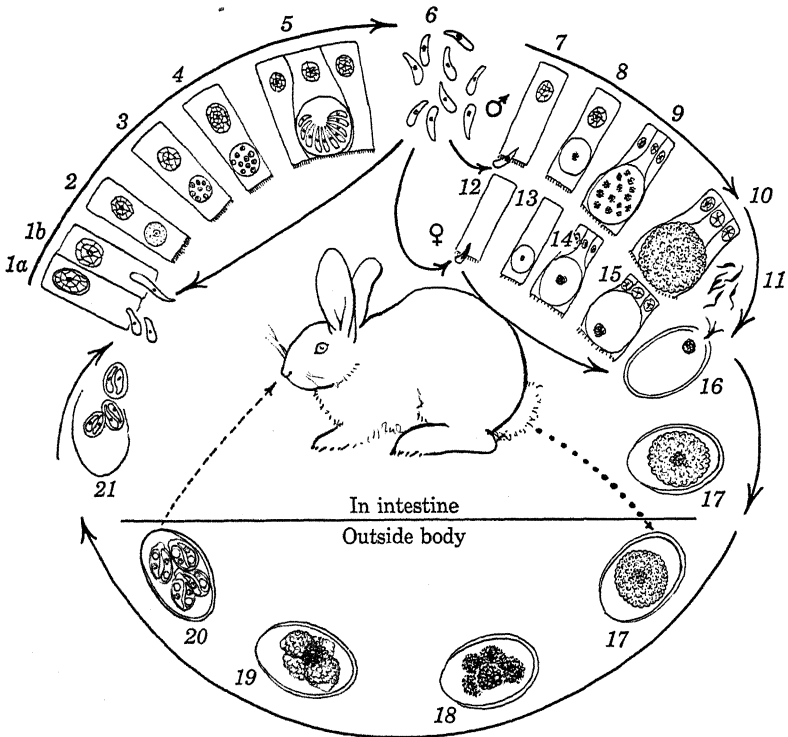


FIG. 51. Life history of *Eimeria perforans* of rabbit. 1a, sporozoite entering intestinal cell; 1b, merozoite entering intestinal cell; 2, developing schizont; 3-5, multiplication of nuclei and formation of merozoites; 6, liberated merozoites, reinfecting other intestinal cells; 7-10, development of ♂ gametocyte; 11, microgametes; 12-15, development of ♀ gametocyte; 16, fertilization of macrogamete; 17, undeveloped oöcyst ready to leave body of rabbit, and after escape with feces; 18-19, formation of sporoblasts; 20, development of sporocysts and sporozoites (ripe oöcyst); 21, escape of sporozoites after ingestion of ripe oöcyst. (Adapted from figures by Becker and by Wetzel.)

The Coccidia are most commonly parasites of the epithelial cells of some parts of the intestine, although some species attack the liver and other organs. The species which cause important infections in domestic animals belong to two genera, *Eimeria* and *Isospora*, which differ from each other mainly in details of development within the oöcysts. The life cycle is graphically shown in Fig. 51. After one, two, or more schizogonic cycles the merozoites develop into gametocytes, usually in the same type of cells in which the schizogony occurred. The

microgametocytes produce a swarm of minute two-flagellated microgametes which fertilize the macrogametes, usually after the latter have escaped from the cells which mothered them. The macrogametes are provided with cyst walls but have a small opening called a micropyle at one end through which the microgametes are able to enter. The resulting zygote is a young oöcyst, ready for escape from the host in which it was developed, and prepared to withstand conditions in the outside world until opportunity to enter another host is afforded.

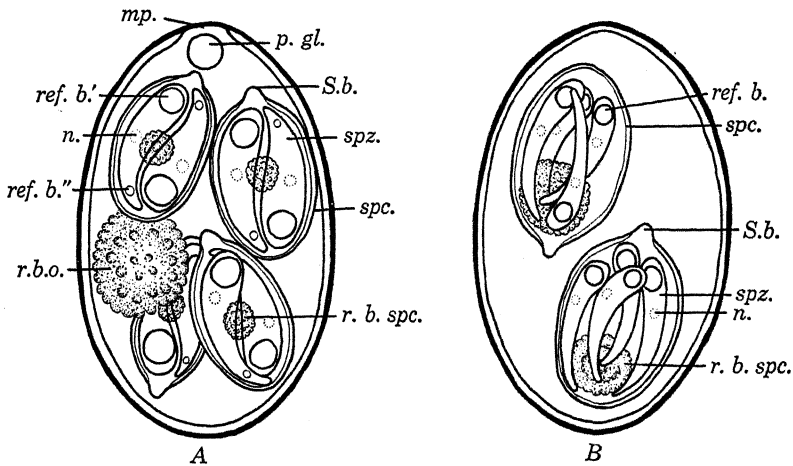


FIG. 52. Diagrammatic representation of oöcysts of *Eimeria* (A) and *Isospora* (B); mp., micropyle; n., nucleus of sporozoite; p.gl., polar globule; r.b.c., residual body of oöcyst; ref.b., refractile bodies of sporozoites; r.b.spc., residual body of sporocyst; S.b., Stieda body or "plug" of sporocyst; spc., sporocyst; spz., sporozoite. (Adapted from Boughton and Volk, *Bird Banding*, 9, 1938.)

In most species the oöcysts (Fig. 53A) are undeveloped when they leave the host with the feces and require 30 hours to 2 weeks to develop, depending upon the species and the temperature. Development takes place in two steps, (1) a division of the nucleus and cytoplasm into a number of parts called sporoblasts, often leaving a residual mass of cytoplasm which may subsequently disappear, and (2) the further development of these sporoblasts into sporocysts with resistant cyst walls, and the division of their contents into a number of sporozoites; sometimes each sporocyst has a residual mass of cytoplasm of its own. The sporocysts are cysts within cysts, and in some species may be liberated from the parent oöcysts before re-entering a host. In the genus *Eimeria* each oöcyst produces 4 sporocysts each with 2 sporozoites (Fig. 52A), whereas in the genus *Isospora* each oöcyst produces 2 sporocysts each with 4 sporozoites (Fig. 52B).

The oöcysts are easily destroyed by a temperature of about 50°C., by desiccation, and by extreme cold, but are highly resistant to chemicals. They can be cultured in the laboratory in a 2 to 5 per cent dichromate or a 1 per cent chromic acid solution. It is startling to find them undergoing development in fixed and stained slides!

The sporozoites liberated from ingested oöcysts penetrate cells in their chosen sites of development, grow into schizonts, and then divide into a cluster of spindle-shaped merozoites, usually about 16 to 30, but

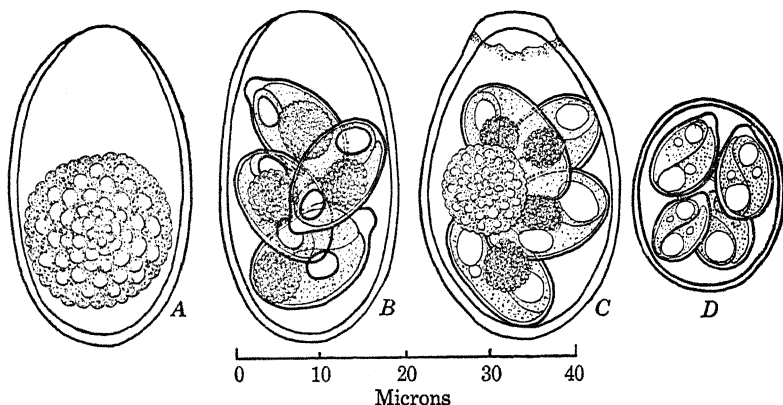


FIG. 53. Various types of oöcysts of *Eimeria*. A, unsporulated oöcyst of *E. stiedae* of liver of rabbit; B, ripe oöcyst of *E. stiedae* with residual bodies in sporocysts but not in oöcyst; C, ripe oöcyst of *E. magna* of intestine of rabbit, with residual bodies in both oöcyst and sporocysts; D., *E. tenella* of cecum of chickens, with no residual bodies. (A to C after Kessel and Jankiewicz, *Am. J. Hyg.*, 14, 1931.)

in the deadly *E. tenella* of chicks about 900, and in *E. bovis* of cattle over 100,000. In most coccidians two or more generations of schizonts are produced before the sexual forms are developed, but in most if not all species the number of schizogonic generations is limited, and therefore continuation of the disease depends on repeated reinfections.

Eimeria bovis of cattle differs from typical species of *Eimeria* in producing a single generation of huge schizonts, 250 to 400 μ in diameter, easily visible to the naked eye, and containing over 100,000 merozoites. The sporozoites begin their development in endothelial instead of epithelial cells; the schizonts mature in 14 to 18 days and then occupy the outer portion of the interior of badly bulged villi. Obviously, with such prolific schizonts, one generation of them is enough. Although the schizonts of this species occur in the small intestine, the gametocytes and oöcysts develop in the cecum and colon; the pathological effects and symptoms are associated only with the latter.

The true nature of these huge schizonts has only recently been determined (Hammond et al., 1946). Similar organisms occur in horses, sheep, and camels and were formerly recognized under the names *Globidium* or *Gastrocystis*. When the life cycles of more of these are determined it may be desirable to separate them from the genus *Eimeria*.

Species. The Coccidia comprise numerous species, most of which show marked host specificity; *Isospora* shows more laxity in its choice of hosts than *Eimeria*. Not only do most species inhabit only a single

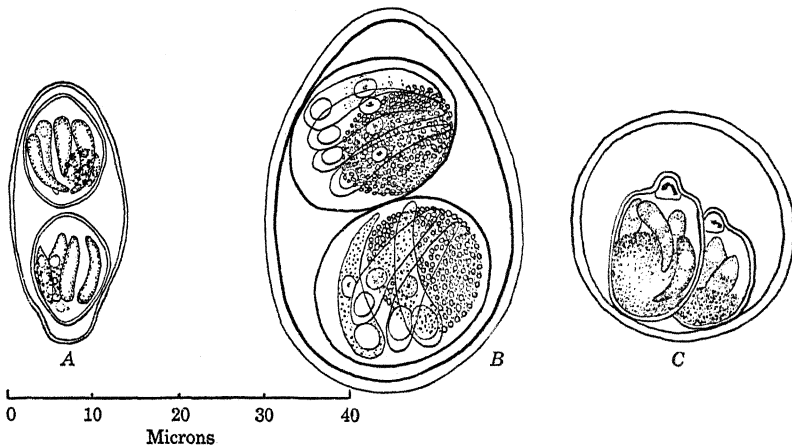


FIG. 54. Oöcysts of three species of *Isospora*. A, *I. belli* of man (after Haughwout, *Philip. J. Sci.*, 18, 1921); B, *I. felis* of cats (after Wenyon, *Protozoology*, 1926); C, *I. lacazii* of sparrows (after Becker, *Coccidia and Coccidiosis*, 1934).

kind of animal or a few closely related ones, but also a single animal may harbor several different species of Coccidia. Members of the genus *Eimeria* have made themselves at home in almost every kind of vertebrate, especially herbivorous ones, and in some invertebrates. In cold-blooded animals the oöcysts mature before leaving the host; in warm-blooded ones they usually mature afterwards. Intestinal forms are very common in rodents, pigs, ruminants, and poultry, and one species is common in the liver of rabbits. *Isospora* is common in small birds (Fig. 54C); Boughton reported references to its occurrences in 173 species, mostly passerines, but whether these represent one or many species is unknown. English sparrows show a very high incidence of infection, especially in the southern states. Canaries suffer from the infection but chickens do not; the latter are afflicted only by *Eimeria*. Among mammals species of *Isospora* are especially frequent in carnivores but are also reported from man, pig, and hedgehog.

Chickens harbor at least 8 species of *Eimeria*, cattle 6, rabbits 6, and pigeons 1; dogs harbor 3 species of *Isospora*, all of which are shared by cats and foxes. Only *Isospora* occurs in man, three species having been reported.

The various species of *Coccidia* vary in the site and developmental details of their schizogonic cycle but are nearly always identifiable by the oöcysts alone, which is fortunate since these are the only forms commonly seen. The principal characters used in distinguishing the oöcysts of different species are size and shape of entire oöcysts, size and shape of sporocysts, the distinctness of the micropyle, the presence or absence of residual bodies in the oöcyst and in the sporocysts, and the thickness of the oöcyst wall.

Ingestion of oöcysts of "foreign" coccidians, passing through the alimentary canal intact, may lead to errors of interpretation. Species which are parasitic in the liver of herrings and in the testes of sardines, for example, have been mistakenly described as human parasites, and it is possible that some of the reported *Eimeria* infections in man may have been pseudo-infections from eating rabbit livers infected with *E. stiedae* (Fig. 53A, B). Passage of the oöcysts through insusceptible animals may serve as a means of distribution.

Human Infections. Although only a few hundred cases of *Isospora* infections in man have been reported, the infection is undoubtedly much commoner in many unsanitary countries than that would suggest. Most of the cases have been reported from the Middle East, Africa, Southwest Pacific, Japan, and South America. In Sao Paulo, Brazil, *Isospora* oöcysts were found in 0.1 per cent of the stools examined, and a somewhat similar incidence occurs in Egyptian villages near Cairo.

Isospora hominis and *I. belli*, both reported from man, were long merged together under the former name, but recent work by Elsdon-Dew in Africa and by Meira and Correa in Sao Paulo supports the view that these are quite distinct species. Both occur in the United States. *I. hominis* has oöcysts that are ovoid and measure about 16 to 10 μ , with developed sporocysts when passed; it closely resembles *I. bigemina* of dogs and may actually be that species. *I. belli* has larger oöcysts, undeveloped when passed, that measure 25 to 33 by 13 to 16 μ , and are definitely narrower at one end (Fig. 54A). This seems to be much the commonest species in man. A third species, *I. natalensis*, with oöcysts about 30 by 25 by 21 μ , and somewhat resembling *I. rivolta* of dogs, was reported once from an African in Natal by Elsdon-Dew. After leaving the body the oöcysts of *I. belli* develop 2 sporocysts each with 4 sporozoites, packed like sardines in a tin, within 24 to 72 hours.

There is evidence that both these species develop in the duodenum or perhaps even in the bile duct. In 28 cases in Sao Paulo, 13 had large, immature oöcysts of *I. belli*, whereas 15 had small, mature oöcysts of *I. hominis*. In Chile all of 11 cases studied were *I. belli*.

Mild diarrhea with light-colored, fatty stools, abdominal distress, and eosinophilia are commonly described in connection with human infections, but some infections seem to be without symptoms. In experimental infections diarrhea and fever appear in about a week. The infections appear to be self-limited and last only a few weeks.

Infections in Animals. In animals the pathogenic effect varies considerably with different species and with the severity of the infection. In light cases there are often no symptoms, but in severe attacks by pathogenic species there is extensive destruction of the epithelium in the chosen sites, with sloughing of the walls and severe hemorrhage. The symptoms are loss of appetite, emaciation, weakness, pallor, diarrhea, bloody feces, and sometimes fever. Animals develop immunity from repeated sublethal infections, but much more quickly and permanently against some species than against others. The immunity is local in nature, with no relation to antibodies in the blood.

Chickens harbor eight species of *Eimeria*; fortunately most of them are mildly pathogenic, but *E. tenella* (Fig. 53D) and *E. necatrix* are very harmful, the former causing severe injury to the ceca in young chicks, with often fatal bloody diarrhea, the latter a more chronic intestinal disease in older birds, characterized by leg weakness, pallor, and general unthriftiness. In cattle several species are pathogenic, including *E. zurnii*, *E. bovis*, and *E. alabamensis*. *E. bovis* has a cycle of development in the host of 20 days and produces huge schizonts visible to the naked eye with merozoite families numbering over 100,000 (see p. 222), *E. alabamensis* has a cycle of 8 to 12 days and produces modest merozoite families of 16 or less. Almost all calves in the southern states are infected; if heavily infected they suffer red or watery diarrhea, weakness, and emaciation, which is often fatal. Other species of Coccidia harmful to domestic animals are *E. meleagriditis* in turkeys, *E. truncata* in geese, *E. deblickei* in pigs, *E. solipedum* and *E. ungulata* in horses, and *Isospora bigemina* in dogs.

Treatment and Prevention. A number of drugs are capable of preventing infection if given with food or water prior to establishment of the infection, e.g., sulfur, certain organic sulfur compounds, and many sulfa drugs (sulfonamides), especially Sulfaquinoxaline. The last has therapeutic effect against *E. bovis* in cattle but not against *E. alabamensis*, presumably because the abundant merozoites of the former are

more exposed while making their way to the large intestine where the sexual stages develop, while the few merozoites of *E. alabamensis* immediately enter neighboring cells (Boughton, 1943).

Sulfa drugs with a pyrimidine nucleus (Sulfadiazine, Sulfamethazine, and Sulfamerazine especially) have been found to have curative as well as preventive action against cecal coccidiosis in chickens (*E. tenella*) if given as soon as symptoms appear, or before. However, since symptoms do not usually appear until the fifth day after infection, and 90 per cent of the mortality occurs by the end of the seventh day, there is not time for much procrastination. These drugs, added to the food at the rate of 0.5 to 2 per cent for 3 days, beginning within 4 days after infection, greatly reduce mortality in chicks (Swales, 1946). Addition of 2 grams of sodium Sulfamerazine per quart of drinking water for 3 days is also effective and perhaps better, since infected chicks lose their appetites but not their desire for water. Sulfaquinoxaline at the rate of 0.05 per cent of the food, given intermittently, or one-fourth that dose continuously, effectively controls *Eimeria tenella* and *E. necatrix* infections in chicks, reducing deaths from over 17 per cent to 1 or 2 per cent. It prevents development of later stages if given up to the fourth day after infection.

About all a harassed poultryman or animal raiser can do to hold in check the ravages of coccidiosis is to try by sanitary means to limit the ingestion of oöcysts to a number that will lead to immunity rather than death, and to utilize the sulfa drugs in food or water as soon as evidence of infection appears. Methyl bromide applied at the rate of 0.15 to 0.3 cc. per sq. ft. of litter or soil inactivates oöcysts. It can also be used as a space fumigant in brooder houses; 2 lb. per 1000 cu. ft. prevents infection.

ARTHROPOD-BORNE ORGANISMS OTHER THAN PROTOZOA

In this section we shall briefly discuss the organisms or disease agents other than spirochetes and Protozoa that are commonly transmitted biologically by arthropods, in order to give a more comprehensive view of them and a better understanding of their relations to each other and to their arthropod hosts than could be obtained from discussions of them in the chapters dealing with the various vectors. Four groups will be considered: the rickettsias and related forms; the *Bartonella-Anaplasma* group of organisms; the filtrable viruses; and the bacteria, among which only the genus *Pasteurella* is biologically transmitted. As far as is known at present no fungus infections are habitually transmitted by arthropods.

Rickettsia and Related Organisms

General Characters. Rickettsias, which are minute organisms believed to be related to bacteria, are strictly intracellular parasites and, like filtrable viruses, have not yet been cultivated except in the presence of living cells in tissue cultures or chick embryos. This is evidently because, again like filtrable viruses, they are degenerate parasites which have become dependent on host cells for essential enzymes. They vary in form, being coccus-like, rod-shaped, or filamentous, and they do not stain readily with aniline dyes as do bacteria, but respond well to Giemsa's stain as do Protozoa. Their primary habitat is in the tissues of arthropods, where some have become necessary commensals; in the hosts to which they are well adapted they cause no apparent disturbance and may be transovarially transmitted generation after generation, e.g., in ticks, but in hosts to which they are poorly adapted they may cause fatal infections, e.g., the rickettsia of epidemic typhus in lice.

Vertebrate infections are undoubtedly a secondary development, resulting when rickettsias in a blood-sucking arthropod are inoculated into a vertebrate and are able to multiply there. Sometimes the infections may then be passed to other individuals without the arthropods being further concerned, as in Q fever infections. In vertebrate hosts the organisms multiply principally in endothelial cells of blood and lymph vessels and in cells lining serous cavities.

The typical rickettsias belong to a family, Rickettsiaceae, the species and classification of which have been reviewed by Bengtson (1948), the nomenclature by Philip (1953). They are arranged in three genera, *Rickettsia*, *Coxiella*, and *Cowdria*.

The genus *Rickettsia* contains non-filterable coccus-like or rod-shaped organisms, less than half a micron in diameter, which cause typhus-like diseases in man. Those of one group, recognized by Philip as a subgenus *Dermacentroxenus*, multiply in the nuclei as well as in the cytoplasm of cells in both the mammal and arthropod hosts; they are the cause of a group of diseases known as spotted fever, tick typhus, etc., which are transmitted by ticks, and also one species, *R. akari*, that causes a disease known as rickettsialpox, transmitted by dermanyssid mites (see p. 538). Species of another group, subgenus *Rickettsia*, multiply only in the cytoplasm of cells, and are transmitted by fleas and lice, in which there is no transovarial transmission. To this group belong *R. typhi*, which causes the flea-borne, endemic or murine typhus, and *R. prowazekii*, the cause of louse-borne epidemic typhus, and perhaps also *R. quintana*, a species which causes trench fever, but which

differs in regularly multiplying extracellularly in the intestine of lice (see p. 609). A third group, subgenus *Zinsera*, contains one species, *R. tsutsugamushi*, which causes scrub typhus and is transmitted by the larvae of trombiculid mites (redbugs), being transovarially transmitted in these mites. In addition to its different mode of transmission it differs from the typical rickettsias in other minor characters (see Bengtson, 1948).

The genus *Coxiella* contains a single species, *C. burnetii*, which causes Q fever of man and animals. It is characterized by multiplying in the cytoplasm of mammalian cells, but *outside* the cells in arthropods, and in being filtrable. It multiplies in all kinds of ticks, but also in fleas, lice, and bugs. It is not transovarially transmitted by arthropods, and is commonly transmitted by such agents as dust, milk, meat, etc.

The genus *Cowdria* also contains only one species, *C. ruminantium*, which causes "heartwater" of ruminants, and is transmitted by ticks, not, however, transovarially.

In addition to these rickettsias there are other organisms which have been included with them, but they (and their affinities) are less well known. These include a few species pathogenic in mammals and transmitted by ticks (*R. bovis* in cattle; *R. canis* in dogs; *R. suis* in pigs) which are sometimes placed in the genus *Ehrlichia*; a species, *Neorickettsia helmintheca*, resembling *R. canis*, which causes salmon-poisoning and is transmitted by a trematode (see p. 320); and a number of species from arthropods, some of which are symbionts.

Typical Rickettsial Diseases. The typical rickettsias cause typhus or typhus-like diseases which are transmitted by ticks, mites, fleas, or lice. The diseases of this group all have similar general pathology and clinical character and show various degrees of cross-immunity. In all of them the serum of an immunized animal causes agglutination of certain strains of bacilli of the genus *Proteus*, although these bacteria are in no way related to the rickettsias; this is called a Weil-Felix reaction. In the tick-borne, flea-borne, and louse-borne types of typhus, as well as rickettsialpox, strains called OX19 and OX2 are agglutinated in various titers; in the mite-borne scrub typhus, strain OXK is agglutinated but the others are not.

Characteristic features of the typhus group of diseases are fever, an eruptive rash or purplish spotting of the skin a few days after onset, nervous and often gastro-intestinal symptoms, microscopic nodules around arterioles, and a marked reduction in leucocytes (leucopenia). In some, e.g., scrub typhus and boutonneuse fever, an ulcer develops at the site of the infective bite.

The various forms of tick typhus (see p. 569) caused by the *Der-*

macentroxenus group are certainly closely related, although several groups are sufficiently distinctive so that their rickettsias are dignified by separate species names, e.g., *R. rickettsii* of spotted fever in North and South America; *R. conorii* of boutonneuse fever in the Mediterranean region, and similar if not identical tick-borne, typhus-like diseases of Central and South Africa and India; and *R. australis* of North Queensland tick typhus. The parasite of rickettsialpox also belongs to *Dermacentroxenus*, although its vectors are mites instead of ticks (see p. 538).

There is likewise a close relationship between flea-borne endemic or murine typhus (see p. 633) and louse-borne epidemic typhus (see p. 607); they differ principally in their effects on laboratory animals. There is some evidence that either one of these types may revert to the other. The flea-borne type is undoubtedly the primitive one, from which the louse-borne type developed when lice originally acquired the rickettsias from human beings who were accidentally infected by rat fleas, for lice invariably die from typhus infections, whereas fleas do not appear to be inconvenienced. However, transovarial transmission does not occur even in fleas, so one may speculate that possibly a tick- or mite-borne type was the parent of the flea-borne type and the grandparent of the louse-borne type.

Scrub typhus (see p. 535), transmitted by larval trombiculid mites (redbugs) and called by various names in different parts of the Orient, is immunologically a distinct type, though clinically it resembles other typhus diseases. In 1946 a rickettsia resembling that of scrub typhus, and thought to be transmitted by *Trombicula microti*, was found infecting numerous meadow mice (*Microtus*) on an island in the St. Lawrence near Quebec. No human infections have been observed.

Unlike most virus diseases, the rickettsial diseases are susceptible to treatment with certain antibiotics, particularly Terramycin, but also chloramphenicol (Chloromycetin) and Aureomycin to a somewhat less degree. Patients who are treated with these drugs 7 days or more after onset of the disease never relapse, whereas those treated earlier sometimes do so temporarily. This suggests that the antibiotics do not directly kill the organisms but suppress them for a number of days until the patient has time to mobilize his own defensive mechanism. A high degree of protection against the typhus-like diseases is obtained by vaccination with killed rickettsias grown in chick-embryo yolk sacs, in ticks or lice, or in lungs of intranasally inoculated animals.

Other Rickettsial Diseases. Q fever (see p. 574), as noted above, is caused by a filtrable rickettsia, *Coxiella burnetii*. This disease was probably originally tick-borne, and thus transmitted among wild

animals, but it is secondarily transmitted, particularly to man, by contact with cattle or their feces or dried urine, by unpasteurized milk, or by inhaled dust or droplets. In this disease pneumonic symptoms are prominent and there is no rash. Q fever is susceptible to treatment with Terramycin but not with the other antibiotics.

Salmon poisoning, long thought to be a fluke-transmitted virus (see p. 320), was shown by Cordy and Gorham (1950) to be caused by a rickettsia-like organism, *Neorickettsia helmintheca*.

Heartwater fever, caused by *Cowdria ruminantium*, that differs somewhat from other rickettsias morphologically, is a disease of cattle, sheep, and goats in South Africa, transmitted by ticks. The most characteristic symptom is accumulation of fluid in the pericardium.

In addition to these forms, rickettsias or rickettsia-like organisms have been described from Bullis fever (see p. 574) and trench fever (see p. 609) in man and from African East Coast fever of animals. Elementary bodies of a number of filtrable viruses (see p. 231) have also been interpreted by some workers as rickettsias. Actually, the borderline between rickettsias and filtrable viruses with visible elementary bodies is becoming increasingly obscure, as Philip (1943) pointed out. All the arthropod-borne rickettsial diseases are discussed further under their respective vectors.

BARTONELLA-ANAPLASMA GROUP (BARTONELLACEAE)

These minute organisms, like the rickettsias, stain poorly with aniline dyes, but well with Giemsa's stain. They parasitize the red blood cells of man and other mammals, and some, at least, have arthropod vectors. Some were once classed with Protozoa, but they show no distinct cytoplasm or other typical protozoan characters. The included organisms are as follows:

1. *Anaplasma*, which causes severe and often fatal disease of cattle, characterized by fever and intense anemia. Appears as minute round, deep-staining dots, about $1\ \mu$ in diameter in red corpuscles (Fig. 43M). Is transmitted by ticks (see p. 577) but also mechanically by instruments in dehorning, interrupted feeding of biting flies, etc.

2. *Eperythrozoon*, species of which cause somewhat less severe disease in a variety of animals, including ictero-anemia of pigs. Somewhat resembles *Anaplasma*, but stains blue or violet instead of red. One species, in rodents, is known to be transmitted by a louse.

3. *Grahamella*, bacteria-like bodies that stain light blue with darker areas at the poles, in corpuscles of moles; the same or similar forms reported in many other animals. Pathogenic to moles and rodents.

4. *Haemobartonella*, minute coccus or bacillary forms scattered on surface of red cells of many animals; cause disease only after splenectomy, are eliminated by arsenical drugs, and are cultivated on artificial media with difficulty.

One species, *H. muris*, is practically universal in wild and most strains of laboratory rats, but demonstrable only after splenectomy. Transmission by fleas, lice, bugs, etc.

5. *Bartonella*, which multiplies in endothelial cells as well as in red blood cells. Cultivable on cell-free media. Includes one species, *B. bacilliformis*, the cause of Oroya fever and verruga peruviana of man in South America (see p. 653). Transmitted by sandflies (*Phlebotomus*).

Of these organisms, *Anaplasma* was the last to be evicted from the Protozoa, where it was long thrown in with the Haemosporidia for want of a better place to put it. De Roberts and Epstein (1951) showed by electromicrography that it reproduces by budding off numerous particles of submicroscopic size; these scatter in the corpuscles and presumably are liberated in the blood to infect other corpuscles.

Filtrable Viruses

A considerable number of important human diseases have causative agents so small that they are beyond the range of visibility and will pass through filters which will hold back any microscopically visible organisms. These filtrable viruses are probably not primitive forms of life but highly degenerate forms that have become more and more dependent on the cells in which they live to provide them with enzymes and materials that free-living organisms provide for themselves. The intracellular rickettsias and some of the largest viruses, e.g., vaccinia, are only a little less complex than bacteria, but the process of loss and of concomitant decrease in size continues until in the smallest and simplest viruses, like those of tobacco mosaic and poliomyelitis, little or nothing is left but naked nucleoprotein molecules which have inherent in them the power of reproduction. The host cells provide all the necessary enzymes and materials. In many ways the simplest viruses are comparable with genes both in size and properties, differing mainly in the ability to move from cell to cell. Like genes they are subject to mutation.

Although not a natural group, all viruses have certain features in common. They are more resistant to antiseptics than bacteria. They all tend to stimulate the cells in which they grow to increased multiplication, followed by death of the cells, but the necrosis may occur too rapidly for the growth stimulus to be apparent, and this is the only observed effect in nerve cells, which cannot multiply. Many produce "inclusion bodies" which are in reality masses of the elementary filtrable bodies. As noted on p. 230, some of the larger of these elementary bodies are not unlike rickettsias, and those of trachoma, psittacosis, and lymphogranuloma have been so interpreted. Sometimes the masses of elementary bodies are surrounded by a mantle of amorphous material

produced by cellular reaction, suggesting Protozoa, for which a special class "Chlamydozoa" (mantled animals) was once proposed. All viruses stimulate formation of neutralizing antibodies which inactivate them and thereby provide the most commonly used method for identifying them.

An attempt has been made by Holmes (1948) to classify viruses and give them genus and species names as for other organisms. He grouped them in three suborders to include the viruses that affect bacteria, plants, and animals, respectively. The genera have received such intriguing names as *Erro* (encephalitis), *Legio* (poliomyelitis), *Formido* (rabies), *Charon* (yellow fever), *Tarpeia* (influenza and colds), *Tortor* (hog cholera), *Molitor* (warts), and *Rabula* (pox).

The viruses of vertebrates that are primarily arthropod-borne fall reasonably well into two principal groups. One contains forms that are primarily "visceral"; these produce fevers, sometimes a rash, and a marked decrease in leucocytes (leucopenia). Yellow fever, Rift Valley fever, dengue, sandfly fever, and Colorado tick fever belong to this group. The second group contains forms that are neurotropic at least to the extent that their most serious pathogenic effects are on the central nervous system, although in a high percentage of cases, as in poliomyelitis, these neural symptoms may not appear at all; to this group belong the encephalomyelitis viruses (see pp. 233-234). The distinction between these two groups is not, however, very sharp, for neurotropic strains of yellow fever and dengue have been produced in the laboratory, and there are many viruses in tropical Africa and South America which show no sharp tendency to be either viscerotropic or neurotropic, or whose affinities are very imperfectly known, if at all. Good examples are the West Nile and Ntaya viruses of Africa (see p. 733).

In addition to the groups of viruses discussed in the last paragraph there are a number of others that may be transmitted by arthropods but are not primarily dependent on them, such as fowlpox of birds and swamp fever of horses.

It is still uncertain what role arthropods play in transmission of poliomyelitis, but the epidemiology strongly suggests their implication. The disease is prevalent in summer, is more frequent in small towns and edges of cities than in the centers of them, and does not spread in crowds. Flies harbor the virus, which they acquire from human feces, and monkeys eating food contaminated by infected flies show evidence of infection by developing neutralizing antibodies, as do a large percentage of human beings when an outbreak occurs, but there is no paralysis. Furthermore, fly-controlled areas in south Texas had as high

an incidence of polio cases as did uncontrolled areas. Might it not be possible that infection via the digestive system by small doses of virus deposited on food by flies may lead to immunity without paralysis? The absence of the virus from the blood argues against arthropods acquiring it by sucking blood, although they might possibly inoculate it if infected in some other way. The writer wonders whether mosquitoes like *Culex* might not acquire the virus from sewage-polluted water as larvae, and subsequently inoculate it after becoming adults.

Of the first group of primarily arthropod-borne virus diseases mentioned above, yellow fever is the most severe and is the only one causing mortality. It is transmitted by mosquitoes, although an instance of experimental transmission to a monkey by a mite has been reported. The disease is discussed in more detail on p. 720. The virus is present in the blood of patients for only 3 days and requires about 10 days for a mosquito to become infective, after which it persists for life, although it is not transovarially transmitted. Dengue fever (see p. 727), of which there are at least three distinct antigenic types, is also transmitted only by mosquitoes, but the evidence is conflicting as to how long it takes for mosquitoes to become infective and whether transovarial transmission can occur (see p. 728). Sandfly fever is very similar to dengue but is transmitted only by *Phlebotomus papatasi*, in which it is transovarially transmitted; at least two antigenic types exist. Colorado tick fever (see p. 577) is also very similar to dengue but is transmitted by ticks; transovarial infection occurs. Rift Valley Fever of east central Africa is a severe disease of sheep but mild in man; it also affects cattle, monkeys, and rodents. It is believed to be transmitted by mosquitoes.

Of the group of arthropod-borne viruses causing encephalomyelitis or encephalitis, sometimes erroneously called sleeping sickness, there are many mosquito-transmitted strains (see p. 731). Three strains are common in the United States and Canada—eastern and western equine and St. Louis encephalomyelitis; several in South America, including Venezuelan and Argentinian; two in the Far East, Japanese B, and Russian spring-summer encephalitis; one in Australia, Murray Valley; and about a dozen, distinct from all the others, in Africa, of which West Nile and Ntaya are commonest. All appear to be primarily mosquito borne and are discussed further on pp. 731 to 734, except the Russian spring-summer disease, which is transmitted by ticks and is discussed on p. 577. As Warren pointed out in 1946, there is a very close relationship between the virus of this disease and that of louping ill in sheep; the former commonly attacks man in Siberia, and the latter is a disease of sheep in Russia and northern Britain.

The North American encephalitides can also infect mites, which for a while were thought to be important as reservoirs to carry them through winters and between epidemics. Eklund (1954) called attention to the fact that temperate-zone encephalitis viruses are primarily transmitted by *Culex* and involve birds extensively, whereas tropical viruses, including yellow fever and dengue as well as the neurotropic ones, are primarily transmitted by *Aedes* or other mosquitoes and not primarily by *Culex*, and that the principal vertebrate hosts are always mammals rather than birds. It has been suggested that the temperate-zone viruses may depend for survival on migration of their bird reservoirs.

Little is known about transmission of viruses by helminths, but this is a subject worthy of further investigation. The virus of swine influenza is transmitted by a nematode lungworm (see p. 437), and that of lymphocytic choriomeningitis has been shown to be transmissible by *Trichinella* larvae. It is possible that such diseases as poliomyelitis, ornithosis (psittacosis), and other viruses which are abundant in the intestine, might be transmitted by eggs of intestinal worms.

ARTHROPOD-BORNE BACTERIA

Although a few bacteria are able to cause disease in arthropods, the latter, particularly some of the blood suckers, are remarkably resistant to the establishment and multiplication of most bacteria other than the atypical spirochetes and rickettsias. In many species, e.g., bedbugs, lice, and some ticks, the intestine contains potent bactericidal properties and may be completely sterile, whereas the intestines of others are packed with particular kinds of bacteria (see Steinhaus, 1946). In many insects, e.g., flies, roaches, and ticks, the intestine may harbor various bacteria (such as those of anthrax and the intestinal group causing typhoid, dysentery, and food poisoning) long enough for them to pass through and be voided in the feces, sometimes perhaps with a little multiplication en route; however, such infections do not persist. In the case of ticks such infections are often transmitted while the tick is biting. *Ornithodoros* and fleas have been found to harbor *Salmonella enteritidis* and to transmit it to experimental animals; ticks, bedbugs, and fleas may be vectors of brucellosis (see pp. 575, 588). The tick *Dermacentor albopictus* has been shown to harbor a bacterium, *Klebsiella paralytica*, that causes a disease of moose.

The only typical bacteria which establish themselves, multiply, and persist in arthropods, so that the arthropods act as true biological transmitters, are two species of the genus *Pasteurella*: *P. pestis*, the cause of plague, and *P. tularensis*, the cause of tularemia. These are small,

non-motile, non-spore-forming bacilli which stain deeply at the ends (bipolar staining). *P. pestis*, when ingested by fleas with the blood of an infected animal, multiplies so prodigiously in the esophagus, proventriculus, and stomach that it frequently blocks the alimentary canal, but it does not invade other parts of the body and does not multiply in any other insects. *P. tularensis*, on the other hand, can be transmitted by a variety of arthropods, including ticks, deerflies, lice, bedbugs, and fleas. However, there is little doubt that ticks are the primary arthropod hosts. Unlike *P. pestis* in fleas, *P. tularensis* invades the hemocoel in ticks and is transovarially transmitted. Plague is discussed further on pp. 629-633, and tularemia on pp. 574-575.

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Part II HELMINTHOLOGY



Introduction to the "Worms"

Classification. The name "worm" is an indefinite though suggestive term popularly applied to any elongated creeping thing that is not obviously something else. There is hardly a branch or phylum of the animal kingdom that does not contain members to which the term worm has been applied, not excepting even the Chordata. In fact some animals, such as many insects, are "worms" during one phase of their life history and something quite different during another.

In a more restricted sense the name worm, or preferably helminth, is applied to a few phyla of animals, all of which superficially resemble one another in being unquestionably "worm-like," though in life and structure they are widely different. In fact, man has more in common with a salamander than a nematode has with a tapeworm. The helminths which are of interest to us as parasites of vertebrates belong to four different phyla of the animal kingdom, the Platyhelminthes or flatworms, the Acanthocephala or spiny-headed worms, the Nemathelminthes or roundworms, and the Annelida (or Annulata), the segmented worms including the leeches.

The relative importance of the major groups of helminths may be roughly judged by Stoll's 1947 estimate that there exist in the world today, among some 2200 million people, 72 million cestode, 148 million trematode, and over 2000 million nematode infections. Of course, like money and brains, these are not evenly distributed among the individuals!

Platyhelminthes. This phylum contains the helminths of lowest organization. The great majority of them are flattened from the dorsal to the ventral side, hence the common name flatworm. Unlike nearly all other many-celled animals they have no body cavity, the organs being embedded in a sort of spongy "parenchyma" or packing tissue. The digestive tract in its simplest form, and as it occurs in the asexual

generation of flukes known as *rediae*, consists of a blind sac with only a single opening, serving both as a mouth and as a vent, but in most adult forms this sac is variously branched and in a few flukes even has an anus. On the other hand, the tapeworms have dispensed with the digestive tract entirely, food being absorbed through the outer surface of the body, some from the contents of the lumen of the intestine in

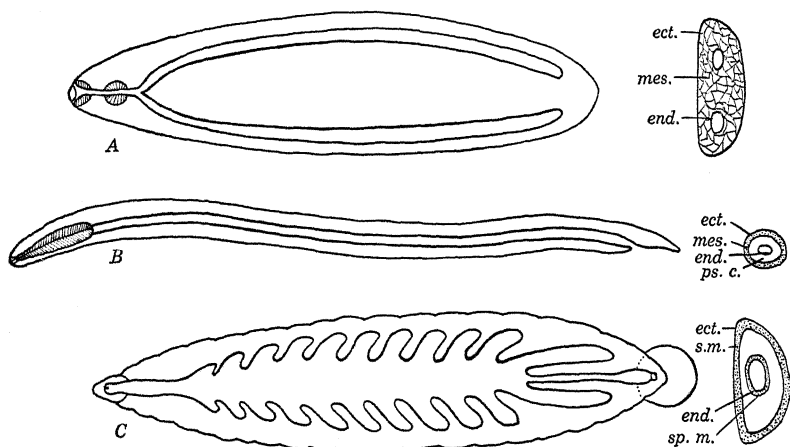


FIG. 55. Diagrams of digestive tracts and cross-sections of bodies of representatives of Platyhelminthes (*A*); Nemathelminthes (*B*); and Annelida (*C*). *A*, fluke; gut branched into two ceca, no anus and no body cavity. *B*, nematode; gut a simple tube with only pharynx differentiated, anus present, body cavity a pseudo-celome not lined by splanchnic mesoderm internally. *C*, leech; gut with ceca for surplus food, anus present, body cavity a true celome lined by splanchnic mesoderm internally and somatic mesoderm externally. Abbreviations: *ect.*, ectoderm; *end.*, endoderm; *mes.*, mesoderm; *ps.c.*, pseudo-celome; *s.m.*, somatic mesoderm; *sp.m.*, splanchnic mesoderm.

which they live, some from the mucous membrane with which they are in contact. The nervous system is very simple, and the primitive ganglia which serve as a brain are located in the anterior portion of the worm. Performing the function of kidneys is a system of tubes, the terminal branches of which are closed by "flame cells," so called from the flame-like flickering of a brush of cilia which keeps up a flow of fluid toward the larger branches of the system and ultimately to the excretory pore, thus conducting the waste products out of the body.

The most highly developed systems of organs, occupying a large portion of the body, are those concerned with reproduction. All but a few of the Platyhelminthes are hermaphroditic, containing complete male and female systems in each individual; in tapeworms both systems are usually complete in each segment and there may even be double

sets in each segment. In addition to the ordinary sexual reproduction of the adults, many flukes and tapeworms have special asexual methods of multiplication in the course of their life cycles.

The flatworms are usually divided into three classes, the Turbellaria, the Trematoda, and the Cestoidea, but some zoologists include also the Nemertea, a group of band-shaped marine worms of uncertain relationships, none of which are of interest in connection with human parasitology.

The Turbellaria are ciliated and for the most part free-living animals; they include the "planarians," which can be found creeping on the underside of stones in ponds. The Trematoda include the flukes, all of which are parasitic, some externally on aquatic animals, others internally on aquatic or land animals. They are soft-bodied, usually flattened animals, commonly oval or leaf-shaped, and furnished with suckers for adhering to their hosts. The flukes that live as external parasites of aquatic animals have a comparatively simple life history, whereas those that are internal parasites have a complex life history, including two or three asexual generations, and involving two, three, or even four different hosts.

The third class, the Cestoidea or tapeworms, with the exception of one primitive family living in the body cavity of ganoid fishes, and the members of one genus which are able to complete their development precociously in annelid worms, are (in the adult stage) invariably parasites of the digestive tracts of vertebrate animals and are profoundly modified for this kind of an existence. Except for a few evolutionarily precocious forms in the genus *Hymenolepis* (see p. 363), all tapeworms begin their development in an alternative host, which may be either a vertebrate or an invertebrate. Sometimes two or even three intermediate hosts are involved in the life cycle. Although in some forms a number of adults may develop from one larva as the result of a budding process, there is never an alternation of generations such as occurs in most trematodes. In one subclass, the Cestodaria, the adult worms are single individuals, suggestive of gutless flukes; in the other subclass, Cestoda, all but the members of a single family (Caryophyllaeidae) consist of chains of segments.

Nemathelminthes. This phylum name has been used in the past to include various assemblages of organisms, of which only the class Nematoda has always been present; the Nemathelminthes once included not only the Acanthocephala but even the gregarines (see p. 180). Because of this, Hyman (1951), who includes six classes in this phylum, prefers the less shopworn name "Aschelminthes." She defines the phylum as mostly worm-like, bilaterally symmetrical, unsegmented ani-

mals provided with a body cavity (not a true coelom), with a digestive tract lacking a definite muscular wall and with both a mouth and anus, and no respiratory or circulatory systems. In addition to the Nematoda, five other classes are included, all of them unknown to the average layman, and most of them even to zoologists who have not by some odd chance been attracted to them; they are (1) the rotifers, (2) the gastrotrichs, (3) the kinorhynchs and echinoderans, (4) the priapulids, and (5) the horsehair worms (Gordiacea or Nematomorpha). The last class, Gordiacea, are the only ones likely to attract attention as "worms"; the name "horsehair worm" comes from a popular idea, not yet dead, that they develop out of horsehairs that fall into water. They are very long and slender hair-like worms that live as parasites in insects until almost mature, when they emerge from the insects and reproduce in water or soil. Occasionally they are accidentally swallowed with drinking water and are usually promptly vomited, much to the surprise and horror of the temporarily infested person.

The true nematodes are cylindrical or spindle-shaped worms covered by a very resistant cuticle; they have a simple digestive tract with mouth and anus, a fluid-filled body cavity which is not lined by epithelium as in other animals; and usually separate sexes, with the sex glands continuous with their ducts in the form of slender tubules. There is an excretory system consisting of a glandular apparatus opening through an anteriorly situated excretory pore, in some forms connected with longitudinal lateral canals. The development is always direct and simple but sometimes requires two hosts for its completion.

Acanthocephala. The spiny-headed worms were long included in the Nemathelminthes, but they have little in common with the nematodes in either structure or development; they constitute a very aberrant and sharply defined group of parasites of vertebrate animals. They are characterized by having a large body cavity, complete lack of a digestive tract, a spiny proboscis retractile into a sac, and separate sexes with reproductive systems of unique character (see Chapter 16). The development, which involves an arthropod intermediate host, more nearly resembles that of flatworms than that of nematodes. For the present it seems best to recognize Acanthocephala as a distinct phylum with affinities closer to the cestodes than to nematodes, as Van Cleave did in 1948.

Annelids. The most highly organized group of helminths is the phylum Annelida, including the earthworms, leeches, etc. In three important respects these worms are the first animals in the scale of evolution to develop the type of structure characteristic of the vertebrate animals, namely, a division of the body into segments, the pres-

ence of a blood system, and the presence of "nephridia"—primitive excretory organs of the same fundamental type as the kidneys of higher animals. In addition the digestive system is highly developed and there is a well-developed nervous system with a primitive brain in the head. In some annelids the sexes are separate, though in others both reproductive systems occur in the same individual.

Three classes of Annelida are usually recognized, of which one, the Hirudinea, or leeches, are of interest as bloodsuckers. These differ from other annelids in lacking setae, in the possession of suckers for adhering, and in the fact that the external annulation of the body does not correspond exactly to the true internal segmentation. These animals superficially resemble flukes, so much so that liver flukes are often referred to as liver leeches, but they can be distinguished externally by the segmentation of the body and internally by their totally different anatomy. Both sexes are represented in the same individual.

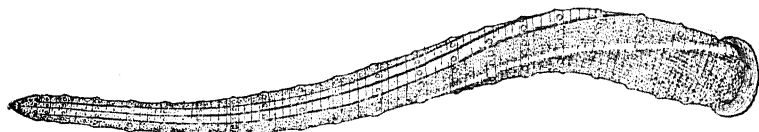


FIG. 56. Japanese land leech, *Haemadipsa japonica*, extended. $\times 2$. (Adapted from Whitman, *Quart. J. Micr. Sci.*, 26, 1886.)

Every boy who has experienced the delights of hanging his clothes on a hickory limb and immersing his naked body in a muddy-bottomed river or pond is familiar with leeches. These are related to the medicinal leeches that were an important stock in trade of medieval physicians, for whom blood-letting was as important as transfusions are to modern physicians. Still more familiar with them is any tourist who has journeyed on foot through the jungles of Ceylon, Sumatra, or Borneo, or through the warm moist valleys of the Himalayas or Andes, for hordes of bloodthirsty land leeches infest these places. In southwest Asia *Haemadipsa zeylandica* causes much loss of blood as well as ulceration and inflammation of the bites, which continue to bleed even after the leeches are filled to repletion and drop off. Clothing impregnated with the U. S. Army repellent (see p. 519) is protective against them.

Thirsty horses, and occasionally men, gulping water from pools or streams in Palestine, North Africa, and China, may suffer severe or even fatal loss of blood, and sometimes strangulation, from the settling of "horse leeches" of the genera *Limnatis* or *Haemopsis* in the pharynx or nasal passages or sometimes in urinary passages, where they may hang on for days or months (Masterson, 1908). Another aquatic

leech, *Dinobdella ferox*, is a serious pest in southeastern Asia (see Chin, 1949). When animals or human beings drink from water infested by it, the young worms quickly enter the nostrils or mouth and loop their way to the back of the pharynx or larynx, where they attach, grow rapidly, and often do much damage. Leeches lodged in the nasopharynx let go when 5 per cent cocaine is sprayed into the nostrils.

Although land leeches are nasty pests in some places, they are not known to be vectors of any human infection. Aquatic leeches serve as intermediate hosts for trypanosomes and Sporozoa of fish, amphibians, and turtles. They affect water birds by entering the nostrils and trachea, causing asphyxiation; by serving as intermediate hosts of flukes; by transmitting fowlpox and possibly other diseases; and by sucking blood from around the vent. As one writer put it, whether a duck is tickled or worried is hard to say, but not having hemorrhoids they presumably do not benefit from the leeches as did mankind thus afflicted in the Middle Ages. Some large leeches in northern United States feed voraciously on large snails and thereby seem to have rendered some lakes free of swimmer's itch (see p. 293). These species do not suck blood from vertebrates.

Parasitic Habitats. Hardly any organ or tissue is exempt from attack by worms of one kind or another. There are flukes parasitic in man which habitually infest the intestine, liver, lungs, and blood vessels, and one species occasionally wanders to the muscles, spleen, brain, and many other organs. In other animals there are species with even more specialized habitats; some inhabit the Eustachian tubes of frogs, the frontal sinuses of polecats, the eye sockets of birds, cysts in the skin of birds, etc. All the adult tapeworms of man are resident in the small intestine, but there are species in sheep and goats and one in rats which habitually live in the bile duct; larval tapeworms are found in a great variety of locations—in the liver, spleen, muscles, subcutaneous tissues, eye, brain, etc.

The majority of the parasitic nematodes of man are resident in the intestine, but the filariae and their relatives inhabit various tissues and internal organs, such as the lymph sinuses and subcutaneous connective tissue. Nematode parasites of other animals, many of which are occasional or accidental in the human body, may occur in all parts of the alimentary canal and in its walls, and in liver, lungs, kidneys, bladder, heart, blood vessels, trachea, peritoneum, skin, eye, and sinuses. None live as adults in the central nervous system, although invasion of it by larvae that have lost their way is a common and sometimes dangerous occurrence. The surface of the body and cavities of the nose and

throat of man are not the habitat of any helminth parasites except leeches and the tongueworms; the latter are really arthropods (see p. 544), although they have much more in common with the helminths.

Physiology. Parasitic worms vary in their diet. Tapeworms, having no alimentary canal, absorb carbohydrates from the intestinal fluid in which they are bathed but obtain nitrogenous and probably other substances from the mucous membranes with which they are in contact (Chandler, 1943). Flukes feed in part on blood and lymph, in part on cells and tissue debris. Some nematodes, e.g., hookworms, feed mainly on blood, but others subsist principally on tissues, either ingesting them and digesting them in the intestine or first liquefying them by the products of esophageal glands. Ability to dissolve tissues is also shared by some flukes. As was shown on pp. 21-24, the tissues seem to be capable of developing resistance to digestion by the worms; this is a reversal of the anti-enzyme armament of the parasites which keeps them from being digested by the host. In hosts immunized by repeated or long-standing infections, intestinal nematodes, unable to feed in the midst of plenty, fail to grow and are soon eliminated.

Although some parasitic helminths live in blood and tissues where there is an abundance of oxygen, and others in the intestine or bile ducts where oxygen is a scarce commodity, all are facultative anaerobes, showing considerable tolerance to absence of oxygen. Some apparently can get along indefinitely at very low oxygen tensions and are injured when exposed to very much of it, whereas others thrive in its absence for only limited periods. All helminths, however, consume oxygen to some extent when it is available, and produce carbon dioxide. It has generally been assumed that the lumen of the intestine of a vertebrate animal is a practically anaerobic environment, but Read (1950) pointed out that the space next to the mucosa may be quite similar physiologically to intercellular spaces inside the host, and may contain considerable amounts of oxygen and other substances that would not be found in appreciable amounts free in the lumen. Competition for the oxygen, or rather for the space where it is available, might be the critical factor concerned in the "crowding effect" in tapeworm infections (Read, 1951). The need for oxygen may be the reason why hookworms have such an insatiable appetite for blood, which is constantly sucked from the host, passed through the body as through a vein, and spilled into the intestine (see p. 422). Most parasite eggs also require oxygen to complete their development.

The intermediary metabolism of helminths, i.e., their techniques for utilizing food materials, disposal of wastes, conversion of one chemical substance into another, etc., apparently involves just as many and just

as complicated enzyme systems as operate in their hosts, but recent work shows that while the helminth enzymes have similar functions, they are chemically different and may not produce the same end products. This is a field of parasitology which is still largely unexplored, but in which there is growing interest. Knowledge of the physiology and biochemistry of helminths may make it possible to find effective anthelmintics by a logical process of reasoning instead of the hit or miss method of trial and error used in the past, for a large proportion of modern chemotherapy, as noted on p. 22, is based on interference with enzyme systems of parasites. Some advances along this line have already been made (see von Brand, 1952). This knowledge may also lead the way to successful artificial cultivation of helminths, which would be of very great help in studying them. Important contributions to the knowledge of helminth physiology and biochemistry have been made in recent years by von Brand, Bueding, Daugherty, and Read in the United States, by van Grembergen in Europe, and by Rogers in Australia.

Although helminths are very poorly equipped with sensory organs, they show amazing ability to react when the necessity arises. With no evident specialized sense organs of any kind whatever a single male *Trichinella* finds a single female in the relatively vast expanses of a rat's intestine; *Clonorchis* larvae almost unerringly discover the minute opening to the bile duct; and miracidia, the larvae of flukes, are attracted by their proper snail hosts as are filings by a magnet.

Life History and Modes of Infection. The life history and modes of infection of worms vary with the habitat in the body. Every parasitic worm must have some method of gaining access to the body of its host and must have some means for the escape of its offspring, either eggs or larvae, from the host's body in order to continue the existence of its race. Many species utilize intermediate hosts as a means of transfer from one host to another; others have a direct life history, i.e., they either develop inside the escaped egg and depend on such agencies as food and water to be transferred to a new host, or they develop into free-living larvae which are swallowed by or burrow into a new host.

Most of the intestinal helminths enter their host by way of the mouth, and the eggs escape with the feces. Many species enter as larvae in the tissues of an intermediate host which is eaten by the final host, e.g., most of the tapeworms, many flukes, and some nematodes (spiruroids). Some nematodes of the intestine, such as the pinworm and whipworm, make their entry as fully developed embryos in the eggs. Others, like the schistosomes, hookworms, and *Strongyloides*, usually reach their destination in an indirect way by burrowing through the skin. All the

intestinal worms except *Trichinella* produce eggs or larvae that escape from the body with the feces. In *Trichinella* the larvae encyst in the muscles, and their salvation depends on their host's being eaten by another animal.

Many of the helminths of other organs of the body also enter by way of the mouth and digestive tract, though they have various means of exit for the eggs or larvae. The liver flukes enter and escape from the body as do intestinal parasites; the schistosomes enter by burrowing through the skin, and the eggs escape with either feces or urine; filariae enter and leave the body by the aid of bloodsucking insects; the guinea worm enters by the mouth, and the larvae leave through the skin. The larval tapeworms which infest man enter either by the mouth or by accidental invasion of the stomach from an adult in the intestine, or, in the case of *Sparganum* infections in China, by the bizarre method of burrowing into the eyes from infected frogs used as poultices. Like those of *Trichinella*, larvae of tapeworms are usually permanently sidetracked in man, and escape only if their hosts have the greater misfortune of being eaten by cannibals, leopards, or rats.

Adjustments in Life Cycles. It is obvious that parasitic worms have a tremendous problem to solve in insuring the safe arrival of their offspring in the bodies of other hosts, on which the survival of the race depends, for sooner or later the body which is affording food and shelter will die, and however immortal the soul may be, the parasites can derive little comfort from it. The problem is difficult enough for worms like *Ascaris*, *Trichuris*, and hookworms, whose offspring merely have to spend a relatively short time in the great outdoors before being ready to return, either as stowaways in food or water or by their own burrowing, to another host of the same species. But flukes and tapeworms are so hampered by heritage and tradition that they have to undergo a preliminary development in some entirely different but often very particular kind of animal, and sometimes must even spend an apprenticeship in a third kind, before they are ready for their ultimate life of ease and comfort in the definitive host. When one considers the experiences through which a lung fluke, for example, must go in order to live and reproduce its kind, first as a minute free-swimming protozoan-like organism, then as an asexually reproducing parasite of certain species of snails, then as a tissue-invading parasite of crabs, and finally as a human invader that must find its way from the stomach to the lungs, he would be incredulous if he were not confronted with the fact that the lung fluke not only succeeds in accomplishing this, but succeeds so well that in some places it constitutes a serious menace to the health of whole communities.

Since the vicissitudes of life for the offspring of parasitic worms are so great, it is obvious that there must be a tremendous waste of offspring which do not succeed in the struggle, and therefore a sufficiently large number of eggs or young must be produced so that the chances of survival are a little greater than the chances of destruction. The numbers necessary to accomplish this are amazing. The hookworm, *Ancylostoma duodenale*, lays in the neighborhood of 20,000 eggs a day, and it may do this for at least 5 years; the total offspring of such a worm would number over 36,000,000. If the number of hookworms in a community remains about constant, as it usually does, and the percentage of males and females is equal, the chances against a male and female hookworm gaining access to a host, and living for the full period of 5 years, is then 18,000,000 to 1. The hookworm, however, has a comparatively simple time of it. Flukes and tapeworms have an even more difficult problem to face. According to estimates of Penfold et al. (1937), a beef tapeworm produces over 2500 million eggs in 10 years, yet this worm is rare enough so that most practitioners keep specimens in bottles on their shelves!

Flukes and tapeworms owe such success as they have to two special devices in their life cycles. In the first place, they have to a large extent substituted self-fertilization for cross-fertilization; they combine male and female organs of reproduction in a single individual and do not take chances on other individuals of the opposite sex being present to render the eggs viable. In the second place, efficient egg-making machines as they are, they have found the production of sufficient eggs by one body inadequate. A tapeworm overcomes the difficulty by constantly reproducing, sometimes for years, more egg-producing segments, in essence new individuals, by a process of budding. Some, such as *Multiceps* and *Echinococcus*, go even further and produce several or even many thousands of buds while in the larval stage, each of which is capable of developing into a new individual when, if ever, it reaches its final host.

Flukes attain the same end in a different way. Instead of producing a sufficient number of eggs to overcome the chances of destruction through the whole cycle of development, they distribute the risk. They produce enough eggs to overcome the chances against their reaching the mollusk which serves as the first intermediate host; then, in order to overcome the odds against them in the subsequent part of the life cycle, the successful individuals reproduce asexually. This is accomplished by a process of multiplication and separation of the germ cells before they cooperate to form a new individual—what zoologists call polyembryony. A single schistosome embryo, after successfully reaching

the liver of a snail, may give birth, by asexual reproduction, to over 100,000 progeny. Without this advantage a schistosome would have to produce thousands of times as many eggs as it does.

Significance of Intermediate Hosts. One might reasonably ask why some worms adhere to the life cycles which they have, when so much simpler ways of reaching their hosts would seem to be available. A fluke which lives as a parasite in the intestine of a bat, for example, would seem to be very ill-advised to select a snail, on which bats do not feed, as an intermediate host, when an insect would serve so much better. Nature is in this respect strangely inconsistent—she is a peculiar mixture of progressiveness and conservatism. In many instances, as we have seen, she has evolved the most intricate specializations both in life cycle and in structure; there are innumerable instances in the animal kingdom of short cuts and detours in life cycles, devised to meet newly developing conditions. On the other hand, there are some short cuts that nature is too conservative to take. It is one of the fundamental precepts of embryology that ontogeny, i.e., the development of the individual, recapitulates phylogeny, which is evolutionary development of the race. Many unnecessary phases are, however, slurred over or greatly altered, and sometimes entirely new phases are interposed to meet the exigencies of the situation, as, for example, the pupa of insects (see p. 508).

Now intermediate hosts, in which partial development occurs, are unquestionably in many instances ancestral hosts. Mollusks are probably to be regarded as the hosts of the redia-like or cercaria-like ancestors of digenetic flukes. In the course of evolution these developed further until they reached the condition of modern flukes. Nature, however, has been too conservative to produce flukes in which the mollusk phase of the phylogeny is omitted in the ontogeny; this is apparently too radical a short cut. The result is that all flukes, with the exception of two species with forked-tailed cercariae, *Cercaria loossi* and *C. hartmanae*, which develops in annelids, must first be molluscan parasites regardless of their final destiny, just as a chicken must have gill slits like a fish before it can have lungs like its parents. Therefore, we have the irrational condition of flukes becoming first parasites of snails, then of insects, and only after sojourns in these animals, parasites of bats or birds. Undoubtedly the earliest method of transfer of flukes to their final hosts was by the eating of the infected mollusks, a method still adhered to by many flukes of mollusk-eating animals. In more highly specialized flukes, however, the cercariae leave the mollusk to encyst on vegetation if the host is a vegetarian, in fishes or other animals if it is carnivorous, or, in the case of the schistosomes, to take

an active instead of a passive attitude and burrow directly into their final hosts.

A somewhat similar course has been followed by tapeworms, which were probably originally parasites of Crustacea, then became parasites of Crustacea-eaters, and eventually parasites of eaters of Crustacea-eaters. The tapeworms, however, seem a little less hidebound by tradition, for some have substituted insects or even mammals for the ancestral Crustacea, and a very few (e.g., *Hymenolepis nana*) have done away with the need for intermediate hosts altogether.

Not all intermediate hosts can be regarded as heritages from the remote past; some are quite clearly secondarily acquired conveniences in the life cycle to facilitate access to a new host. This is true of the mollusk and earthworm hosts of lungworms (see p. 437) and almost certainly of the insect hosts of spirrurid and filarial worms. But as Rothschild and Clay remark in their delightful book *Fleas, Flukes and Cuckoos*, by whatever paths they have evolved, the life cycles of parasitic worms are today sufficiently complicated and extraordinary to satisfy the imagination of Salvador Dali himself. As they say: "When the flatworms gave up their freedom they certainly began an odyssey compared with which the voyages of Ulysses seem singularly uneventful and commonplace."

Host Relations. The effects produced by parasitic worms depend in part on the organs or tissues occupied, in part on the habits of the worms, and in part on the poisonous qualities of their secretions or excretions, in part on the number of worms harbored, and to a very large degree on acquisition of immunity.

Worm infections differ radically from bacterial or protozoan infections in that the worms do not multiply in the body of the host, and thus the infections are quantitative in nature. The bite of a single lightly infected mosquito may produce as severe a case of malaria as numerous bites by heavily infected mosquitoes, but the acquisition of a few hookworms, liver flukes, or filariae produces in a given individual a very different effect from the oft-repeated acquisition of large numbers of these worms. The term "infestation" instead of "infection" is frequently used to distinguish non-multiplying invaders from multiplying ones.

In some instances even single worms may cause a serious disturbance. Thus a single *Dibothriocephalus latus* may cause severe anemia; a single gnathostome may cause a fatal perforation of the stomach wall; a single *Ascaris* may block the bile or pancreatic duct; and a single guinea worm creeping under the skin may lead to an infection causing loss of a limb. In the majority of cases, however, the pathogenicity of worms is proportional to the number present.

Some investigators tend to minimize the damage done by helminths, especially intestinal ones, whereas others undoubtedly overestimate it. Improved facilities for discovering infection have demonstrated the presence of intestinal parasites in so many unsuspected cases that we are likely to incriminate them in nearly every morbid condition for which we cannot, with equal readiness, discover another cause. Differences in the effects of worm infestations are due in part to the variable susceptibility of different races and individuals; in part to presence or absence, and degree, of malnutrition or other debilitating influences; in part to number of worms harbored and rate at which the worm burden is increased; and in part to acquired immunity. If the rate of acquisition of worms is slow enough in a well-nourished individual, immunity can develop before serious damage has been done (see p. 25).

Effects of Parasitism. The principal ways in which helminths harm their hosts are by mechanical damage, devouring of tissues or loss of blood, and by toxic effects. Some large worms, such as the larger tapeworms, may rob the host of enough food, especially proteins or vitamins, to cause malnutrition or mild vitamin deficiencies in hosts that are on a suboptimum intake, especially in the case of young, growing individuals. This is especially striking in infestations with *Dibothriocephalus*; this worm has a special affinity for vitamin B₁₂, and as a result precipitates pernicious anemia in persons who are on the borderline of it (see p. 347).

The mechanical injuries are almost as numerous as the kinds of worms. Some, such as the hookworms, bite the intestinal wall and cause hemorrhages, which are intensified by a secretion which prevents the blood from coagulating; some, such as the lung flukes and guinea worms, cause tissue damage and inflammation by burrowing; some, such as schistosomes and numerous Spirurata (*Gnathostoma*, *Gongylonema*, *Onchocerca*, *Spirocerca*, etc.), cause the formation of tumors, and in some cases—either by irritation or toxic action—of true cancerous growth; some, such as *Ascaris*, may block ducts or even cause intestinal obstruction; some, such as gnathostomes and occasionally *Ascaris*, may cause perforation of the walls of the digestive tract and consequent peritonitis; some, such as the liver flukes, may choke up the bile passages of the liver; some, such as Bancroft's filaria, may interfere with the normal flow of lymph and divert it into abnormal channels; some, such as hydatid cysts, may interfere with the proper functioning of neighboring organs by pressure; some, such as the schistosomes, may produce profound irritation of the tissues by extruding their eggs into them; and some, such as hookworms and spiny-headed worms, open

up portals of entry for bacteria. We have awakened to the importance of a "whole skin" and the danger which accompanies the piercing of it by the unclean proboscides of biting insects. We have not yet fully awakened to the importance of an uninjured mucous membrane. As has been pointed out by Shipley, the intestinal worms play a part within our bodies similar to that played by bloodsucking arthropods on our skins, except that they are *more* dangerous since, after all, only a relatively small number of biting insects have their proboscides soiled by organisms pathogenic to man, whereas the intestinal worms are constantly accompanied by bacteria that are capable of becoming pathogenic if they gain access to the deeper tissues. Weinberg found that, whereas he was unable to infect unparasitized apes with typhoid bacilli, apes infested with tapeworms or whipworms readily contracted typhoid fever, the bacteria presumably gaining entrance through wounds in the mucous membrane made by the worms.

Some effects of worms which were once ascribed to toxic products liberated into the tissues are now known to be caused in other ways, e.g., the primary anemia in hookworm infections, and the pernicious anemia in *Dibothriocephalus* infections. Probably all worms that live in the blood or tissues, however, sensitize the body to their secretions or excretions, or to their body substance, and this causes allergic reactions. These are largely responsible for the symptoms in infestations with such adult worms as the filarias, schistosomes, and guinea worms, with the migrating larvae of such worms as *Trichinella*, *Strongyloides*, hookworms, and *Ascaris*, and even with such adult worms in the intestine as *Ascaris* and *Enterobius*.

A characteristic feature of an allergic reaction is an increase in the number of eosinophiles. These are white blood corpuscles containing granules that stain red with eosin. Such an increase in eosinophiles (called eosinophilia) is one of the most characteristic features of helminthic infection, particularly during the period when the helminths are developing or migrating in the body. From a normal of 1 or 2 per cent of the leucocytes, the eosinophiles may rise to 5 per cent or more, sometimes to 75 per cent, in infections with *Trichinella*, schistosomes, *Echinococcus* cysts, etc. There is some evidence that ACTH may alleviate severe allergic reactions sufficiently to be a life saver in severe *Trichinella* infections (Davis and Most, 1951).

Diagnosis. The diagnosis of infection with various species of worms depends principally on the identification of their eggs or larvae as found in the feces or other excretions by microscopic examination. Nearly every species of parasite has recognizably distinct characteristics of the eggs, the chief variations being in size, shape, color, thickness of shell,

stage in development, appearance of the embryo if present, and presence or absence of an operculum or lid.

In many instances whole groups of worms have egg characteristics in common; for example, the eggs of flukes, except schistosomes, have an operculum at one end; those of schistosomes have spines; those of most tapeworms of warm-blooded animals have no operculum and contain a fully developed six-hooked embryo. Those of *Dibothriocephalus*, however, and most of the tapeworms of cold-blooded animals, have undeveloped operculated eggs like those of flukes; eggs of the tapeworm family *Taeniidae* are characterized by thick inner shells (embryophores) which have a striated appearance in optical section; eggs of ascarids are thick shelled, bile stained, and with surface markings; those of whipworms and their allies are brown with an opercular plug at each end; those of oxyurids are colorless and flattened on one side; and those of the hookworms and all their allies of the suborder Strongylata have thin-shelled, unstained eggs without either opercula or surface markings. Some eggs of the commoner worms are shown in a comparative way in Fig. 57.

Most worm infections of the digestive system can be diagnosed by finding eggs or larvae in the feces, but this cannot be relied on in some kinds of infections. Tapeworms, other than *Dibothriocephalus* and its allies, have no natural exit for the eggs from the segments, but in most species the eggs are easily released from ruptures of the uterus at the ends of the detached ripe segments. *Hymenolepis* eggs are probably always released inside the body and become mixed with the feces. *Taenia saginata* eggs are more frequently found on the skin near the anus, since the detached segments often squirm out of the rectum. However, infections with the larger tapeworms are best discovered by examining the surface of freshly passed stools for the segments, which squirm actively like flukes (for which they are sometimes mistaken). Pinworms (*Enterobius*) do not ordinarily deposit the eggs in the feces at all; the females crawl out of the anus and deposit the eggs on the perianal skin, where they can be picked up by special devices described on p. 451. *Trichinella*, since its embryos do not normally leave the body at all, cannot often be diagnosed by fecal examination, though sometimes some of the adult worms can be expelled by violent purges or anthelmintics. For this and some other helminthic diseases—filariasis, infestations with larval tapeworms, and schistosomiasis—skin tests or other immunological tests must often be resorted to; these will be discussed in connection with the diseases concerned.

Intestinal worm infestations can usually be diagnosed by finding eggs or larvae, though the number present may vary considerably from

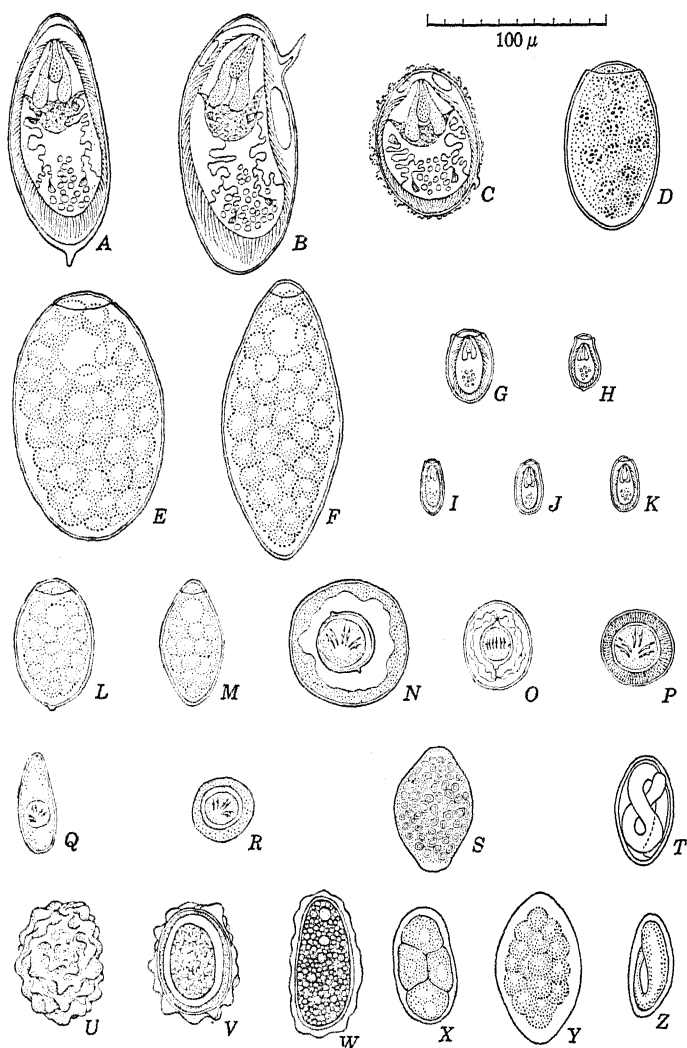


FIG. 57. Eggs of parasitic worms, drawn to scale ($\times 250$). Flukes: A, *Schistosoma haematobium*; B, *Schistosoma mansoni*; C, *Schistosoma japonicum*; D, *Paragonimus westermani*; E, *Fasciolopsis buski*; F, *Gastrodiscoides hominis*; G, *Dicrocoelium dendriticum*; H, *Clonorchis sinensis*; I, *Opisthorchis felinus*; J, *Heterophyes heterophyes*; K, *Metagonimus yokogawai*. Tapeworms: L, *Dibothriocephalus latus*; M, *Spirometra mansonoides*; N, *Hymenolepis diminuta*; O, *Hymenolepis nana*; P, *Taenia* sp. or *Echinicoccus*; Q, *Raillietina madagascariensis*; R, *Dipylidium caninum*. Nematodes: S, *Diectophyma renale*; T, *Gongylonema* sp.; U, *Ascaris lumbricoides* (surface view); V, Same, optical section; W, Same, unfertilized; X, *Necator americanus*; Y, *Trichostrongylus* sp.; Z, *Enterobius vermicularis*.

day to day. In heavy infestations microscopic examination of a simple smear in water, thin enough to read newspaper print through, is sufficient, but many light infestations escape detection by this method and concentration methods are necessary.

Flotation methods in heavy salt or sugar solutions are valuable for eggs of most kinds of nematodes and some tapeworms but fail to float the eggs of schistosomes, the operculated eggs of flukes or *Dibothriocephalus*, the porous eggs of tapeworms of the family Taeniidae, the eggs of *Acanthocephala*, or the unfertilized eggs of *Ascaris*.

One of the best techniques for demonstration of these eggs, particularly those of intestinal schistosomes, is a modification of the old Telemann acid-ether technique, known as the AMS III method (Hunter et al., 1948), performed as follows:

1. Comminute 2 grams of stool with 5 cc. of an equal mixture of HCl (40 cc. concentrated HCl in 60 cc. of water) and sodium sulfate (sp. gr. 1.08).
2. Strain through gauze moistened with this mixture, pour into a 15 cc. centrifuge tube, and wash two or three times by centrifuging for about 1 minute at 2000 r.p.m., decanting the supernatant fluid each time and mixing the sediment with fresh mixture.
3. Add 5 cc. of fresh mixture plus 3 drops of Triton NE (a detergent) plus 5 cc. refrigerated ether, shake for 30 seconds, and centrifuge for 1 minute.
4. Remove tube, loosen ring of debris at interface of ether and HCl-Na₂SO₄ mixture with applicator stick, and decant.
5. Swab tube down to the sediment with cotton swab.
6. Add physiologic saline to the 0.4 cc. mark, mix sediment, pipette onto 1 or 2 slides, apply cover glass, and examine.

Another modification of the Telemann technique, which is good for protozoan cysts as well as eggs, consists of comminution of the stool in saline followed by straining and washing as above, addition of 10 per cent formalin to the sediment, then addition of ether after 5 minutes, followed by steps 4 to 6 above (Ritchie, 1948).

For flotation saturated NaCl (sp. gr. 1.200), or ZnSO₄ (sp. gr. 1.180), which also brings up protozoan cysts, is most frequently used, though a sugar solution is preferred by some. The simplest flotation method is that of Willis (1921), in which a 1-oz. or 2-oz. tin container for collecting fecal samples is left one-sixth to one-tenth full of feces, and is then stirred gradually with salt solution until brimful. A 2 by 3 in. glass slide is then placed over it in contact with the fluid; in 10 minutes the slide is carefully lifted by a straight upward pull, inverted, and examined.

Lane (1928) devised a method of direct centrifugal flotation (DCF). About 1 cc. of stool is thoroughly mixed with water in a centrifuge tube with a ground top, centrifuged, and the supernatant poured off. The

residue is then mixed with saturated NaCl or ZnSO_4 (sp. gr. 1.180), the tube filled to the top, covered with a No. 2 cover glass, and placed in centrifuge buckets provided with four projecting horns to prevent the cover glass from sliding off during the centrifuging. After centrifuging for 1 minute at 1000 rpm, the cover is removed and the adhering fluid examined as a hanging drop or by dropping the cover on a slide. The special apparatus is unnecessary if the last few drops of solution to fill the tube are added after centrifuging, and the surface film is removed by touching a cover to it or by means of a 4-mm. bacteriological loop. The DCF method demonstrates a high percentage of the eggs present, and in a small area.

Egg Counts. About 1920 Darling called attention to the importance of quantitative diagnosis of worm infections. Stoll in 1923 devised a satisfactory method of estimating eggs per gram of feces by diluting a measured quantity of feces in a measured volume of 0.1 *N* NaOH, counting the eggs in a measured fraction, and multiplying by the proper factor. Stoll and Hausheer in 1926 recommended the use of a special narrow-necked flask filled to a 56-cc. mark with 0.1 *N* NaOH, and then to a 60-cc. mark with feces, thus diluting 4 cc. fifteen times. After thorough shaking, the eggs in a 0.075-cc. drop of this are counted under a 25-mm. square cover glass. The eggs counted, multiplied by 200, represent the eggs per gram. The method will not do for very light infections and is unreliable in individual counts, but when averaged, even for small groups, is useful in estimating the worm burden of a community, and in determining the relative number of light, medium, and heavy infections. Adjustments should usually be made to bring the results of the examinations to a uniform basis of formed stools. Egg counts in "mushy" stools are multiplied by two, and in liquid stools by four. Beaver (1949) devised a method by which adjustments for density of stools are made with the help of a light meter (photoelectric cell).

Treatment. Treatment of the various worm infections is considered under the head of the different kinds of worms, but a few general principles should be noted here.

Drugs which are used for expelling worms are known as anthelmintics. An ideal anthelmintic is one which effectively kills or expels the particular worms for which it is used, is not injurious to the host in the dose required, is easily administered, and is cheap.

There is little probability that any anthelmintic will be found that is effective against all kinds of worms, even all intestinal ones. Although nematodes and trematodes, which have digestive tracts, respond to many of the same drugs, tapeworms are affected very little by most

of these drugs, but respond to entirely different ones which have little effect on the other worms. Even among intestinal nematodes susceptibility to drugs varies greatly. Hookworms are easily killed by tetrachlorethylene, but *Necator* more readily than *Ancylostoma*, and *Ascaris* is merely annoyed by it; the reverse holds true to a considerable degree for oil of chenopodium. Phenothiazine is highly effective against *Haemonchus* and moderately so against species of *Trichostrongylus*, but is without significant effect against *Nematodirus*; yet all of these belong to the same family, Trichostrongylidae.

Little is known about the mechanisms by which most anthelmintics exert their effects. Some, e.g., ficin and papain, which are proteolytic enzymes in fresh fig latex and papaya, respectively, digest the tissues of nematodes. Many anthelmintics probably act, as do other chemotherapeutic drugs, by interfering with enzyme systems, e.g., the antimony drugs used against schistosomes, but for the most part the mode of action is unknown. Some drugs exert their effects slowly, and may have sterilizing effects by gradually destroying the reproductive organs, particularly the ovary, e.g., antimony compounds used against schistosomes, and arsenic compounds against filariae. Some antifilarial drugs quickly kill the microfilariae (embryos) and only slowly affect the adult worms, others have the opposite effects. It is quite possible that some of the drugs used against intestinal worms might have similar effects in preventing reproduction by slowly destroying the sex organs if used in small doses over a period of time, but anthelmintics against intestinal worms are usually discarded and considered worthless if they are not immediately lethal.

The fact that animals given commercial Phenothiazine frequently gain weight even though they have very low worm burdens has been interpreted as meaning that these low, subclinical infections are really harmful. It appears now, however, that the gain in weight may actually be due to effects of the drug on the thyroid, resulting in accumulation of fat rather than muscle (Talmage, 1953). This would be satisfactory for farmers marketing beef cattle, but not for owners of race horses. This question certainly needs further investigation.

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The Trematodes or Flukes

I. General Account

The trematodes are animals of a very low order of development in some respects and of very high specialization in others; all of them are parasitic. There are two principal groups: the monogenetic flukes with no asexual generations, which are primarily external or semi-external parasites of aquatic animals; and the digenetic flukes with two or more asexual generations and an alternation of hosts, which are internal parasites of all kinds of vertebrates. Since only the digenetic flukes are of interest as parasites of man and domestic animals, the following account refers to this group except when otherwise specified.

In shape the flukes are usually flat and often leaf-like, with the mouth at the bottom of a muscular sucker, usually at the anterior end; in most groups there is a second sucker, for adhesion, on the ventral surface. The monogenetic flukes have highly specialized compound suckers at the posterior end, usually supplemented with hooks. The thin cuticle of trematodes, often spiny, is apparently secreted by mesodermal cells, since the true ectoderm is lost during development of the cercariae. Under the cuticle are layers of circular, longitudinal and diagonal muscles, and inside of this the loose mesh of the parenchyma.

The development of the nervous system is of low grade; a small ganglion at the forward end of the body gives off a few longitudinal nerves. Sense organs are almost lacking. There is no blood or blood system, the result being that the digestive tract and excretory system are branched, often to a surprising extent, in order to carry food to all parts of the body and to carry waste products out from all parts. The digestive system (Fig. 58) usually has a muscular *pharynx* near the mouth, and then branches into two blind pouches, the *intestinal ceca*. In some of the larger flukes, e.g., *Fasciola hepatica*, these ceca have numerous branches and subbranches, while in the schistosomes the

ceca reunite posteriorly to form a single stem. Only in a few aberrant species do the ceca open posteriorly.

The excretory system consists of a complicated arrangement of branched tubules. At the ends of ultimate fine branches are flame

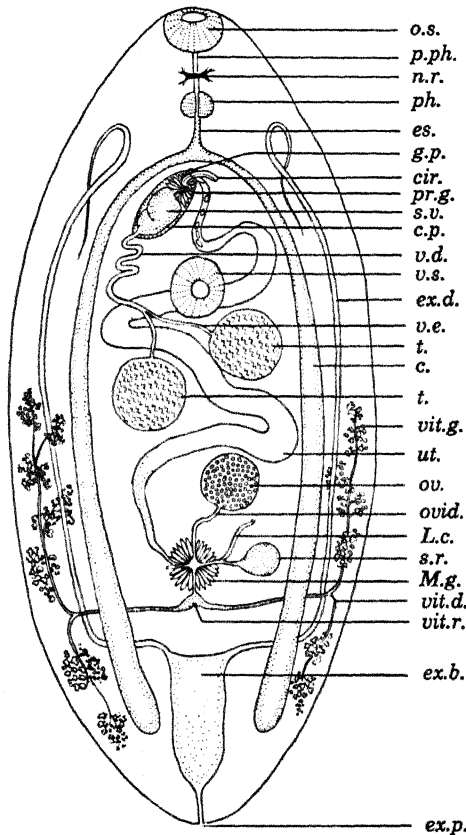


FIG. 58. Diagrammatic fluke to illustrate principal morphological characteristics. Abbreviations: *c.*, cecum; *cir.*, cirrus; *c.p.*, cirrus pouch; *es.*, esophagus; *ex.b.*, excretory bladder; *ex.d.*, excretory duct; *ex.p.*, excretory pore; *g.p.*, genital pore; *L.c.*, Laurer's canal; *M.g.*, Mehlis' gland; *o.s.*, oral sucker; *ov.*, ovary; *ovid.*, oviduct; *ph.*, pharynx; *p.ph.*, prepharynx; *pr.g.*, prostate glands; *s.r.*, seminal receptacle; *s.v.*, seminal vesicle; *t.*, testis; *ut.*, uterus; *v.d.*, vas deferens; *v.e.*, vas efferens; *vit.d.*, vitelline duct; *vit.g.*, vitelline glands; *vit.r.*, vitelline reservoir; *v.s.*, ventral sucker.

cells which keep up a flow of fluid towards the excretory pore. The finer branches unite in a definite manner, varying in different groups. In monogenetic flukes the excretory system opens by two anteriorly placed pores (Fig. 60) but in the digenetic flukes the main collecting

tubules on each side open into a posteriorly situated bladder which in turn opens to the exterior by a single pore (Fig. 59). In digenetic flukes the type of branching of the excretory system is of value in

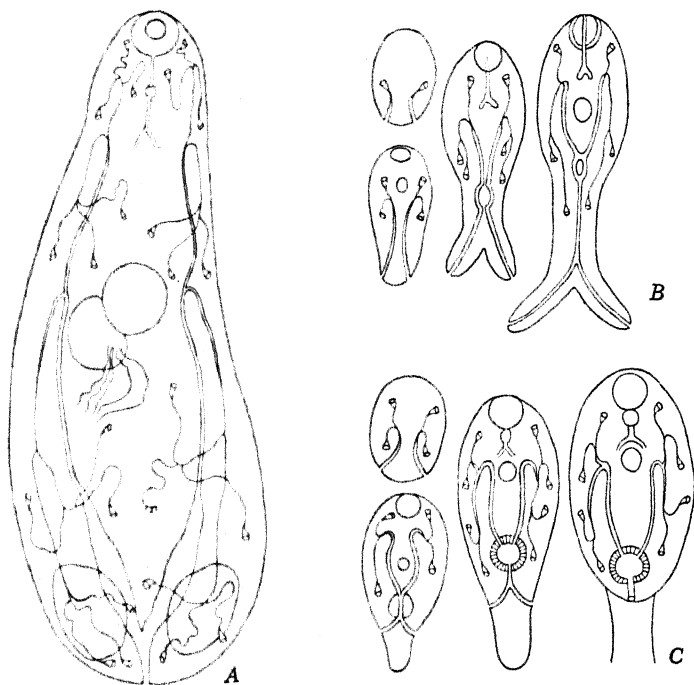


FIG. 59. Excretory system of digenetic flukes. *A*, excretory system of *Heterophyes heterophyes*. Note Y-shaped bladder, division of main collecting ducts at level of ventral sucker, and two groups of 3 flame cells each on both the anterior and posterior branches, giving a flame-cell formula $2[(3+3) + (3+3)]$. *B*, diagram of development of excretory system in Strigeata, showing formation of bladder by fusion of two principal ducts, and primary excretory pores on sides or end of tail. *C*, diagram of development of excretory system in flukes with stilet cercariae, and in Opisthorchioidea showing thick-walled excretory bladder derived from cell mass replacing primitive bladder formed by fusion of main ducts. (*A*, after Looss from Stunkard, *J. Parasitol.*, 1929); *B* and *C* adapted from unpublished sketches by LaRue.)

classification but is difficult to determine in the adults; group differences are more readily determined in the living cercariae, and are even present in the ciliated embryos or miracidia. The flame cell arrangement is commonly expressed in a formula; the arrangement in Fig. 59A is $2[(3+3) + (3+3)]$, indicating that on each side there are two groups, of three flame cells each, on the anterior main branch of the excretory tubule, and two groups, of three each, on the posterior main

branch. The excretory bladder in some flukes is formed by fusion of the two lateral tubules in a developing cercaria and expansion into a bulb (Fig. 59B), and in others from a mass of cells (Fig. 59C).

Some flukes, especially the amphistomes (see p. 312), have a lymphatic system of much-branched, delicate tubules in the parenchyma; this seems to function as a primitive circulatory system.

Few animals have more intricate and highly specialized reproductive systems, and their life histories are so marvelously complex as to tax our credulity. Many flukes, especially those living as internal parasites in land animals, pass through four and sometimes even five distinct phases of existence, during some of which they are free-living, and during others may parasitize successively two, three, or even four different hosts.

In all flukes except those of the family Schistosomatidae and one other family, both male and female reproductive systems occur in the same individual and occupy a large portion of the body of the animal.

In the female system there are separate glands for the production of the ova proper, the yolk and shell material, and the fluid in which the eggs are carried. In a typical digenetic fluke the organs are arranged as diagrammatically shown in Fig. 58, but there are many variations. The *ovary* has a short duct, the *oviduct*, which is joined by a *yolk* or *vitelline duct*, a short duct from a *seminal receptacle* if one is present, and by a duct which leads to a pore on the dorsal surface of the fluke, called *Laurer's canal*. Close to where these various ducts meet there is a slight bulb-like enlargement called an *oötype*, surrounded by a cluster of unicellular glands called *Mehlis' gland* and formerly thought to be a shell gland; it is now known that the shell material comes from granules in the yolk cells.

The oötype is an assembly plant for the production of finished eggs; in some flukes the daily output is estimated at 25,000! The yolk and shell material are provided by clusters of little *vitelline glands* usually situated in the lateral parts of the fluke but occasionally posteriorly or anteriorly. These clusters of glands are connected by ducts to one main transverse duct from either side; these right and left ducts come together to form a common duct shortly before entering the oötype, often with a small *vitelline reservoir* at their junction. Sometimes there is no separate seminal receptacle; instead the sperms are stored in the region of the oötype or lower part of the uterus. Laurer's canal, sometimes connected with the seminal receptacle or its duct instead of directly to the oviduct, is believed to be a vestigial vagina, but in many species it fails to reach the dorsal surface; like the human appen-

dix, it is a useless heirloom. In most flukes it is probable that the sperms make their way down through the uterus before this becomes jammed with eggs.

When the eggs are fertilized, supplied with yolk cells to provide nourishment, and surrounded by shell material which gradually hardens and darkens, they enter the *uterus*. This, usually much coiled and

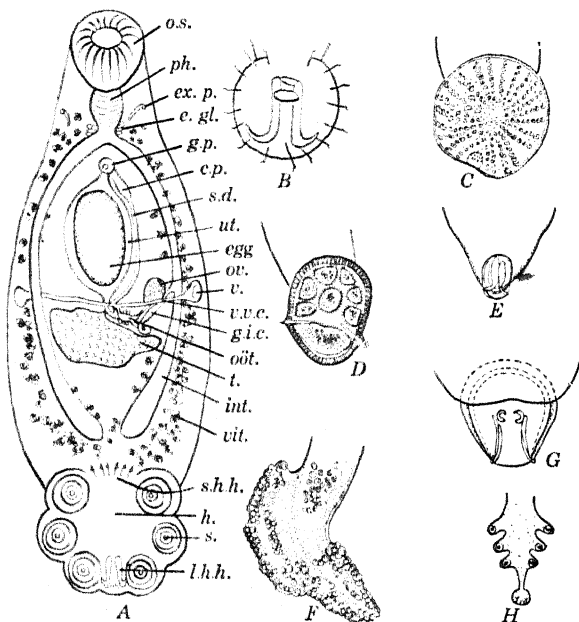


FIG. 60. Monogenea. A, *Polystomoidella oblongum* (Polystomatidae) (after Cable, *Illustrated Lab. Manual of Parasitology*, 1947); B-H, various types of haptors of Monogenea (adapted from various authors); C, Acanthocotylidae; D, Monocotylidae; E, Microbothriidae; F, Microcotylidae; G, Capsalidae; H, Discocotylidae. Abbreviations: c.p., cirrus pouch; e.gl., esophageal glands; ex.p., excretory pore; g.p., genital pore; g.i.c., genito-intestinal canal; h., haptor; int., intestine; l.h.h., large haptorial hooks; oöt., oötype; o.s., oral sucker; ov., ovary; ph., pharynx; s., sucker; s.d., sperm duct; s.h.h., small haptorial hooks; t., testis; ut., uterus; v., vagina; vit., vitellaria; v.v.c., vitellovaginal canal.

convoluted, leads to the *genital pore*, where it opens in common with the male reproductive system. The terminal part of the uterus is often provided with special muscular walls and is called the *metraterm*.

The male system consists of two or more *testes* for the production of the sperms; two sperm ducts which meet to form a *vas deferens*, usually with an enlargement, the *seminal vesicle*, for the storage of sperms; a cluster of *prostate glands*; and a retractile muscular organ or *cirrus* which serves as a copulatory organ. The seminal vesicle,

prostate glands, and cirrus are usually enclosed in a *cirrus sac*. All these complex sex organs in a single animal which may be much smaller than the head of a pin!

Important variations that are of taxonomic value occur in (1) the absolute and relative positions of the ovary and testes; (2) the position of the uterus; (3) the position and arrangement of yolk glands; (4) the presence or absence of a seminal receptacle; (5) the position of the genital pore; (6) the presence or absence of a cirrus sac and the nature of the cirrus; and (7) the presence of a seminal vesicle inside or outside the cirrus sac. The Schistosomatidae, as already noted, are peculiar in having the male and female systems in separate individuals.

The Monogenea differ in their internal structure mainly in (1) having the excretory system of the right and left side separate, opening by two anteriorly situated pores; (2) the testes more variable in number; (3) the presence of a canal connecting the oviduct with the right intestinal cecum in some; and (4) single or paired vaginas or copulation canals in the majority (Fig. 60).

Life Cycle. The more primitive monogenetic flukes, belonging to the orders Monogenea and Aspidobothrea, have a direct development involving a simple metamorphosis but no interpolated non-sexual generations. The Monogenea are parasitic externally or in the excretory bladder or on the gills of aquatic vertebrates, whereas the Aspidobothrea are parasitic on or in the soft parts of mollusks or in the intestines of aquatic vertebrates. Some Aspidobothrea develop to maturity in a single molluscan host, whereas others have achieved an alternation of hosts without an alternation of generations. Flukes of the order Digenea, on the other hand, have very complicated life cycles involving several non-sexual generations which, except in two species, as far as known at present (see p. 249), always develop in snails or bivalve mollusks.

MIRACIDIA. Digenetic flukes produce eggs, often by tens of thousands, which escape from the host's body with the feces, urine, or sputum, according to the habitat of the adults. Either before or after the eggs have escaped from the host ciliated embryos develop within them; these hatch either in water or in the intestines of mollusks which serve as intermediate hosts. The embryos, called miracidia, are free-swimming animals suggestive of ciliated protozoans. They are covered by a ciliated epithelium of relatively few large flat cells (Fig. 61A') and have a short sac-like gut, one or more pairs of penetration glands, one or more pairs of flame cells and excretory tubules, and a cluster of germ cells which are destined to give rise to a new generation of organisms (Fig. 61A). Many miracidia have eye spots, but some are blind.

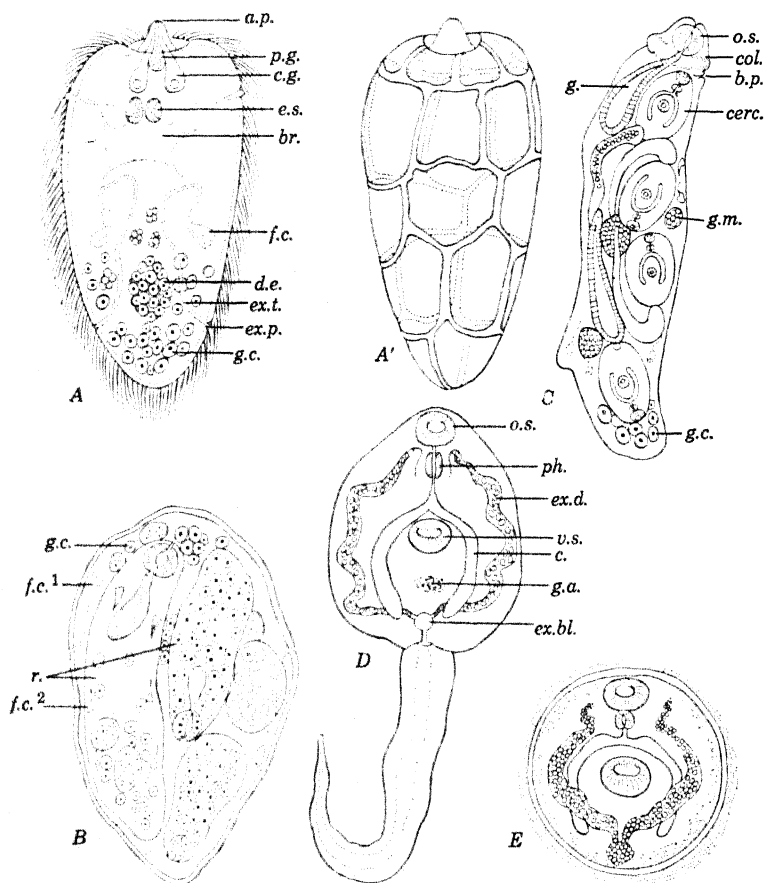


FIG. 61. Stages in life cycle of a fluke. *A*, miracidium showing internal organs, *A'* showing ectodermal cells; *a.p.*, apical papilla; *br.*, brain; *c.g.*, cephalic gland; *d.e.*, developing embryo; *e.s.*, eye spot; *ex.p.*, excretory pore; *ex.t.*, excretory tubule; *f.c.*, flame cell; *g.c.*, germ cells; *p.g.*, primitive gut. *B*, sporocyst; *f.c.¹*, flame cell of sporocyst; *f.c.²*, flame cell of redia; *g.c.*, germ cells; *r.*, developing rediae. *C*, redia; *b.p.*, birth pore; *cerc.*, developing cercaria; *col.*, collar; *g.*, gut; *g.c.*, germ cells; *o.s.*, oral sucker; *g.m.*, germinal mass. *D*, cercaria; *c.*, cecum; *ex.bl.*, excretory bladder; *ex.d.*, excretory duct; *g.a.*, genital anlage; *o.s.*, oral sucker; *ph.*, pharynx; *v.s.*, ventral sucker. *E*, encysted metacercaria.

The miracidia do not feed, and they die in 24 hours or less if unsuccessful in finding a proper molluscan host.

Free miracidia swim in a characteristic spirally rotating manner, in quest of a mollusk of the particular species which is to serve as an intermediate host. When they come very close to such a mollusk they become greatly excited and make a headlong dash for it, although they

ignore other kinds of mollusks. They attach themselves to the soft part of the mollusk by the secretion of their glands and proceed to bore or digest their way into the tissues. Some miracidia, e.g., those of *Clonorchis* and *Dicrocoelium*, hatch only after the eggs have been eaten by the proper snails. It is obvious that only a very small percentage of the embryos are likely to survive the double risk of not reaching water and, if safely in water, of not reaching a suitable mollusk in which to develop.

The miracidia make their way to various tissues of the molluscan host, according to the species, but usually do *not* settle in the digestive gland or liver although that is the commonest site of development for their offspring. The miracidium sheds its coat of flat, ciliated cells and changes in form to become an irregular-shaped, sac-like, filamentous or branched body called a mother sporocyst (Fig. 61*B*). This sporocyst is essentially a germinal sac inside of which are the germ cells, which have descended in a direct line from the original ovum from which the miracidium developed. The germ cells may continue to multiply as single cells or may cluster together to form germinal masses. The latter may then differentiate directly into a new generation of germinal sacs with enclosed germ cells, or may bud these off from their surfaces over a considerable period of time.

DAUGHTER SPOROCYSTS OR REDIAE. This new generation may be simple sacs like the mother and are then called daughter sporocysts, or they may have an oral sucker, sac-like gut, and rudimentary appendages, and are then called rediae (Fig. 61*C*). These emerge from a birth pore in the mother sporocyst and usually make their way to the digestive gland of the mollusk. Here the enclosed germ cells, with or without multiplication as individual cells, again form germ masses which directly develop into a new generation of organisms, or shed partially formed embryos from their surfaces as the cells in the masses continue to multiply.

In some flukes the germ cells in the daughter sporocysts or rediae develop into a structurally different generation, the cercariae, but in some there is a second or even a third generation of rediae before cercariae are produced. In schistosomes and strigeids the mother sporocysts may still be producing daughter sporocysts long after the latter have started producing cercariae; the only limitation to the poly-embryonic capacity of the mother sporocysts seems to be the food and space available in the digestive gland of the snail host, and the daughter sporocysts appear to be able to produce cercariae as long as the snail lives. Thus these reproductive machines may produce up to a million cercariae from a single original egg. There is one record of a snail

that gave off cercariae for 7 years at the rate of over 1,000,000 a year. In some flukes, on the other hand, e.g., *Paragonimus*, a miracidium may end up producing only a few hundred cercariae.

✓ **CERCARIAE.** The cercariae (Fig. 61D) are not germ sacs in which the germ cells multiply and produce new embryos, as are sporocysts and redia. These are true larval forms which undergo no further reproduction in the mollusk, but must by some route, sometimes amazingly devious, reach the final vertebrate host, where they will grow to maturity and reproduce by the more orthodox sexual method.

The cercariae are odd mixtures of features characteristic of the adult flukes into which they will grow, and of special adaptive characters which enable at least a few of them to succeed in the often hazardous transfer from the mollusk where they were born to the vertebrate where they will mature. Usually features connected with the digestive tract, excretory system, and suckers, and a few special features such as the cirrlet of head spines in echinostomes, are prophetic of what type of fluke the cercaria will eventually develop into, but other features are purely adaptive, e.g., the stylet, the tail, the fins, the penetration and/or cystogenous glands, and other features which are sometimes very bizarre. Often certain of these features, together with the few adult characters that may be present, make it possible to predict what the adult of a newly discovered cercaria will be. However, sometimes adult characters that would be expected are absent, e.g., a ventral sucker, or a ventral sucker may be present when absent in the adult.

The cercarial features often give better clues to relationships and correct classification than do the adult flukes. Although nobody would have dreamed of including such widely different adult flukes as schistosomes, strigeids, *Clinostomum*, and gastrostomes (and some others) in one suborder, the strikingly similar features of their miracidia and cercariae (all forked-tailed) make such a grouping unavoidable. Another feature which seems to have been evolved by nature only once is the stylet, a little spine near the oral sucker to help in the penetration of arthropod hosts, so all stylet cercaria belong in one group, even though one would never guess that the adults belong together. Here, however, we run into possible difficulty, for some cercariae without stylets may have secondarily lost them but should nevertheless not be ostracized. Figure 62 gives some idea of nature's uninhibited ideas as to what a cercaria may look like.

All but a few kinds of cercariae have tails; they may be long or short, single or forked (with or without a stem), and with or without fins, bulbs, or other peculiar features; in some the cercaria's body can

be withdrawn into the anterior end of the tail, or the tail may form a cyst from which peculiar appendages protrude. A few cercariae that develop in land snails and couldn't use tails if they had them, have secondarily lost them—such a cercaria is called a cercariaeum.

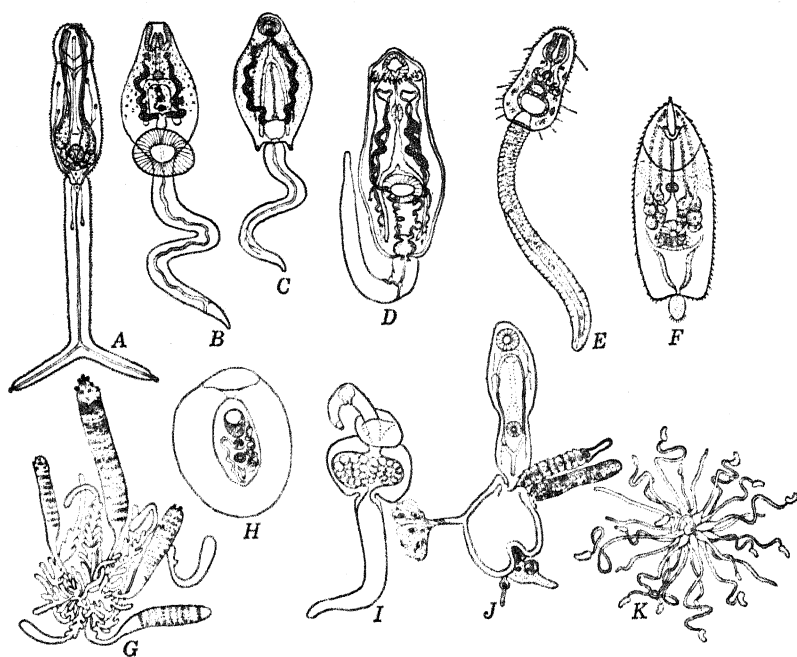


FIG. 62. Some types of cercariae. A, furcocercous (*Schistosoma japonicum*); B, amphistome (*C. inhabilis*); C, monostome (*C. urbanensis*); D, echinostome (*Echinostoma revolutum*); E, pleurolophocercous (*Opisthorchis felineus*); F, stylet, microcercous (*Paragonimus westermani*); G, colored sporocysts of *Leucochloridium paradoxum*, which grow out from tentacles of land snail; H, metacercaria from a sporocyst of *Leucochloridium migranum*, enclosed in jelly-like cyst capsule; I, cystocercous (gorgoderine) (*C. macrocerca*); J, cystophorous (hemiurid), showing cercarial body and various appendages evaginated from tail cyst; K, cluster of "rattenkönig" cercariae (*C. gorgonocephala*). (Adapted from various authors.)

Cercariae usually have one or both of two kinds of glands. Penetration glands are conspicuous features in most, and very useful in identification; they are histolytic and are used for escaping from the snail's tissues, and subsequently for penetrating into intermediate hosts or, in the case of the schistosomes, the final hosts. Many species also have cystogenous glands, the product of which is used in forming cyst walls. These glands are particularly conspicuous in such flukes as *Fasciola*, *Fasciolopsis*, and amphistomes, which encyst on inanimate objects in the

water and form thick protective cysts. Most cercariae do not lead a free existence in water for more than a few days at most.

METACERCARIAE. All flukes except the schistosomes and their near relatives undergo some further development before finally growing into adults. On penetrating a host or preparing to encyst, a cercaria non-

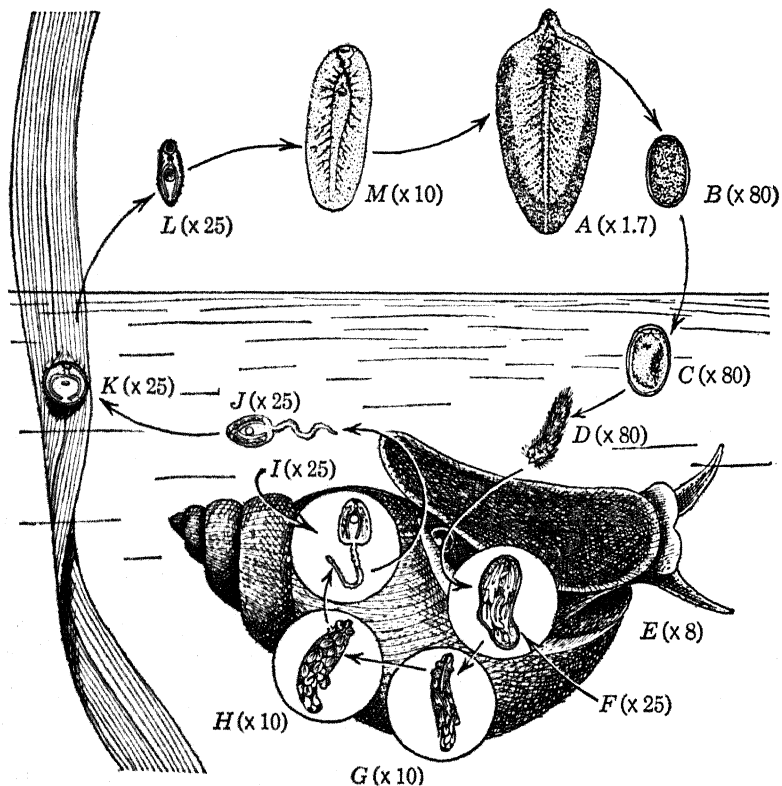


FIG. 63. Life history of liver fluke, *Fasciola hepatica*. A, adult in liver of sheep; B, freshly passed egg; C, egg with developed embryo, ready to hatch in water; D, ciliated embryo in water, about to enter pulmonary chamber of snail (E); F, sporocyst containing rediae; G, redia containing daughter rediae; H, redia of second generation containing cercariae; I, cercaria; J, same, having emerged from snail into water; K, cercaria encysted on blade of grass; L, cercaria liberated from cyst after ingestion by sheep; M, young fluke developing in liver of sheep.

chalantly flips off its tail, exudes the contents of its glands, and proceeds to become a metacercaria (Fig. 61E). In most flukes this metacercarial stage takes place during encystment on vegetation or in an intermediate host, but in some flukes, e.g., some that develop in the humors or lens of the eyes of fishes, they become metacercariae without encysting.

In intermediate hosts the cercarial cyst is usually very delicate and transparent, but the host lays down a fibrous or glassy outer cyst, often conspicuous with pigment granules, which becomes thicker with age.

In some flukes the metacercariae are infective for the final host within a few hours, in others they require days or weeks. In one genus of strigeids (*Alaria*) an additional stage, the mesocercaria, is interposed between the cercaria and the metacercaria, so these flukes require four successive hosts—snails, tadpoles, mice, and mink.

TRANSFER TO FINAL HOST. The manner in which the cercariae accomplish the transfer from snail to final host varies greatly. The self-reliant cercariae of schistosomes actively seek the final host and bore directly into it, but most cercariae depend on the host to pick them up. The simplest method of transfer is encystment directly in the primary mollusk host or even in the mother redia, as happens in some echinostomes. *Leucochloridium* has the cercariae encysted in large colored sporocysts that grow out of the tentacles of snails and resemble tempting worms for birds to peck at (Fig. 62G). In flukes like the Fasciolidae and amphistomes, which reach maturity in herbivorous animals, the cercariae encyst on vegetation in the water and patiently wait to be eaten by the final host. In flukes which mature in carnivorous or insectivorous hosts, the cercariae penetrate into the tissues of frogs, fish, insects, crustacea, etc., where they encyst and await salvation by the second intermediate host being eaten by the final one. It is for this reason that many human fluke infections are prevalent only in the Orient, where fish or crabs are eaten without thorough cooking. Occasionally metacercariae are progenetic, i.e., they become sexually mature before reaching the final host.

The skin-penetrating cercariae of schistosomes are carried to their final destination in the mesenteric blood vessels by the blood stream, but encysted metacercariae always enter by way of the mouth. Their cyst walls are digested away in the intestine, and the young liberated flukes migrate by various routes to the parts of the body in which they are to mature.

Examination of Mollusks for Asexual Generations and Cercariae. When mollusks are collected and brought to the laboratory for examination for immature stages of flukes, those producing cercariae can readily be determined by placing them, first in groups and later individually, in half-pint bottles and leaving them for 12 to 24 hours. The emerged cercariae will then be seen swimming in the water or, in a few instances, crawling on the bottom. In some species all the cercariae emerge almost simultaneously at a certain time of day. Some

are attracted to light, some to the upper layers of the water; and some swim almost continuously, others hang motionless most of the time. The cercariae of some flukes appear only for a short season whereas others continue to emerge for months or even years.

Sporocysts and rediae are found by crushing the mollusks or picking away the shell until the body can be dragged out intact. In most cases they will be found in the brown digestive gland of the mollusk; their presence can often be detected with the naked eye as yellowish mottlings. These must then be dissected out carefully. Cercariae obtained after crushing a mollusk are frequently immature and unlike those escaping naturally. The cercariae, sporocysts, and rediae should be studied in the living state as much as possible, with the help of such intra-vitam stains as neutral red (1:1000) or Nile blue sulfate. Subsequent studies can be made on material fixed and stained by various standard tissue methods.

Molluscan Hosts. The mollusks involved as intermediate hosts of flukes include many families of snails and bivalves, but only snails are involved as hosts for the sporocyst and redia generations of flukes parasitic in man and domestic animals. These include several families of fresh-water snails which have gills and can close their shells by means of an operculum (order Prosobranchia), and both fresh-water and land snails (order Pulmonata), which have a respiratory sac instead of gills, and no operculum.

In the Prosobranchia are included: (1) Hydrobiidae, small aquatic or more often amphibious conical snails containing *Oncomelania* (Fig. 68), hosts of *Schistosoma japonicum*, and *Bulinus* (Fig. 76), *Parafossarulus* (Fig. 74), and *Amnicola*, hosts of the Opisthorchiidae. (2) Thiariidae (formerly Melaniidae), large, high-spired, rough-shelled aquatic snails, containing *Thiara* and *Semisulcospira* (Fig. 70), hosts of *Paragonimus* and *Metagonimus*; *Hua*, of *Clonorchis*; and *Goniobasis*, of *Nanophyetus salmincola*. (3) Potamididae, containing *Pirenella*, host of *Heterophyes heterophyes*; and several marine snails that are hosts for bird schistosomes causing swimmer's itch.

In the Pulmonata are included in the fresh-water group (Basommatophora): (1) Planorbidae (Figs. 68, 85), flatly-coiled snails serving as hosts of *Schistosoma mansoni*, *Fasciolopsis*, and some amphistomes and echinostomes. (2) Lymnaeidae (Fig. 63), dextrally coiled snails serving as hosts of *Fasciola*, and the principal cercariae causing swimmer's itch. (3) Physidae or Bulinidae (see footnote, p. 285) (Fig. 68), sinistrally coiled snails serving as hosts of *Schistosoma haematobium*. In the terrestrial group, Stylommatophora, which have two pairs of head tentacles, are included the hosts of Dicrocoeliidae (*Helicella*,

Cionella [Fig. 73], etc.). For a brief but good review of medically important mollusks, see Mackie, Hunter, and Worth (Section 10).

Classification. The classification of flukes is still in a very uncertain state, as Stunkard (1946) pointed out. The earliest classification was based on the number, position, and character of the suckers, as the names "polystome," "distome," and "monostome" suggest. Later more attention was paid to the details of the internal organs, such as the location and features of the reproductive organs and details of the excretory system. With the development of knowledge of the life cycles of flukes it has become apparent, as LaRue pointed out in 1928, that a taxonomic system which really indicates relationship must be based on comparative anatomy of all the stages in the life cycle and especially of the miracidia and cercariae.

Life-cycle studies, as noted above, have brought some astonishing revelations of previously unsuspected relationships. So many unexpected skeletons in family closets have appeared that some parasitologists are losing faith entirely in the present system of classification. Stunkard (1946), for instance, thinks that in the present state of uncertainty the only groups higher than families in the entire class Trematoda to which one can pin any faith is the division into the two subclasses, Monogenea and Digenea. He thinks that the gasterostomes and Strigeata merge into each other, and the Strigeata into some of the Distomata; and he thinks the separation of Distomata, Monostomata, and Amphistomata is obsolete. The small family Aspidogastridae, parasitic in mollusks, fish, and turtles, is recognized by Faust as a third subclass but is believed by Stunkard to belong with the Digenea, in spite of the fact that it has no asexual reproduction; some species do have an alternation of hosts.

Dawes (1946) agrees with Stunkard in many particulars but does not decimate the long-accepted classification quite so drastically. He divides the Trematoda into three orders, Monogenea, Aspidobothrea, and Digenea, and divides the Digenea into two suborders, Gasterostomata and Prosostomata. In the former the mouth is on the mid-ventral surface, and in the latter at the anterior end.

The gasterostomes also differ in having miracidia with the cilia restricted to comb plates and protruding bars (Fig. 64A) and in having a cercarial tail with long forks but without a stem (Fig. 64B), but in many life cycle features they show so much affinity to other forked-tailed groups that the propriety of separating them into a distinct suborder is questioned. While there is little doubt that all the forked-tailed cercariae belong in one group (Strigeatoidea), and all the stylet cercariae in one (Plagiorchioidea), and certain other families (e.g.,

Heterophyidae and Opisthorchiidae; Fasciolidae, echinostomes, and amphistomes) belong together, there is still so much uncertainty about the limits of these groups that it is better to ignore them for the present as named suborders or superfamilies. Most of the flukes would still have to be grouped as "incertae sedis" or included in the recognized groups with question marks.

Families of flukes containing human parasites are listed below; their characters are given under discussion of the individual families.

Order Monogenea. External or semi-external parasites of aquatic animals; direct development with no asexual multiplication; large posteroventral disc or haptor (Fig. 60), usually armed with hooks or spines and often with pairs of muscular suckers; excretory pores two, anteriorly situated.

Order Aspidobothrea. External or internal parasites of mollusks, fish, or turtles; no asexual multiplication in life cycle but may have alternation of hosts. Rows of sucking alveoli on ventral surface, usually on a large ventral disc. Intestine a single blind sac; excretory pore single, posterior.

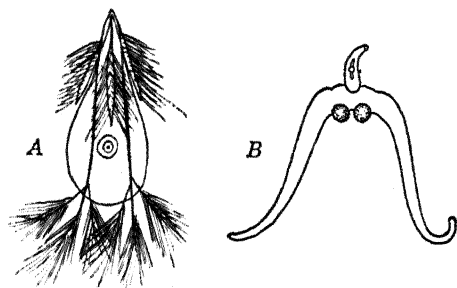


FIG. 64. A, Gasterostome miracidium, and B, cercaria. (A adapted from Woodhead; B from Lühe, *Süßwasserfauna Deutschlands, Trematoda*.)

Order Digenea. Internal parasites; asexual generations interposed in life cycle, nearly always in mollusks; one or two suckers for adhesion; excretory pore single, posterior.

1. **Strigeidae** (p. 323) (holostomes or strigeids). Numerous pathogenic species in intestines of birds and mammals. *Prohemistomum vivax* accidental in man.
2. **Schistosomatidae** (p. 278). Blood parasites of various vertebrates. Three species in man, highly pathogenic. Several species in domestic animals.
3. **Clinostomatidae** (p. 304). Usually in water birds, accidental in man.
4. **Paramphistomatidae** (p. 312). Amphistomes. Common in digestive tract of herbivorous animals; *Watsonius watsoni* rare in man.
5. **Gastrodiscidae** (p. 312). Amphistomes. *Gastrodiscoides* in intestine of man and pigs; *Gastrodiscus* in domestic animals.
6. **Fasciolidae** (pp. 302 and 314). *Fasciola* in liver and *Fasciolopsis* in intestine of man; *Fasciola* and *Fascioloides* important in liver of ruminants.
7. **Echinostomatidae** (p. 321). Echinostomes. A number of species in intestine of man; important in water birds.

8. **Dicrocoeliidae** (p. 305). Important parasites of liver and pancreas of birds and mammals; occasional in man.
9. **Opisthorchiidae** (p. 307). Liver parasites of fish-eating mammals; several genera and species in man.
10. **Heterophyidae** (p. 317). Intestinal parasites of fish-eating mammals and birds. Several genera and species in man.
11. **Troglorematidae** (p. 297). In various locations in birds and mammals. *Paragonimus* in lung of man and fish-eating mammals; *Nanophyetus* carries salmon-poisoning of dogs.
12. **Isoparorchidae** (p. 305). In swim bladder of fishes, one species accidental in man.

The flukes which infect man may be divided for convenience into four groups: (1) the blood flukes or schistosomes, (2) the lung flukes, (3) the liver flukes, and (4) the intestinal flukes. Over forty different species have been recorded as human parasites, but only ten of these are common enough to be more than medical curiosities.

Control. In most cases the most feasible method of control of fluke diseases is destruction of the snails which serve as intermediate hosts. The methods employed depend upon the species of snails involved and on local conditions.

Use of chemical substances is often feasible and offers valuable possibilities. Liver flukes of cattle and sheep do not occur in salty pastures, and a liberal use of salt can under very special conditions be of advantage. The writer (Chandler, 1920) found that all species of snails are destroyed by very high dilutions of copper salts. Since then copper sulfate and copper carbonate have been more extensively employed for destruction of both aquatic and amphibious snails than any other chemicals. Although lime has been advocated for some snails, McMullen and Graham found it of no value against the snail host of *Schistosoma japonicum* in the Philippines, but they found calcium cyanamide a good substitute for copper salts against this snail. Active research is going on to find molluscicides that will be as effective as copper sulfate, but will have longer-lasting effects. This matter is discussed further on pp. 291-292.

Other possible methods of controlling fluke diseases would be by mass treatment and, for man, prevention of pollution of water, and protection against cercariae in the case of schistosomes.

Monogenea

The majority of the monogenetic flukes are parasites of the gills, skin, and cloaca of fishes, but some have established themselves in the urinary bladder of amphibians and in the urinary bladder or mouth cavity of turtles, and one genus is found in the eyes of hippopotamuses.

Some of the species attacking the gills and fins of fishes cause serious losses in fish hatcheries, where they are of much more importance than their endoparasitic relatives. In nature they seldom cause much trouble since there is less opportunity for heavy infections early in life, and a protective immunity develops. Most Monogenea produce large eggs that hatch into larvae which at once attack their definitive hosts, but those of one family, Gyrodactylidae, give birth to larvae of large size, one at a time. *Polystomum* develops either on the gills of tadpoles or in the urinary bladder of adult toads or frogs. Most Monogenea are fairly specific with respect to hosts.

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MONOGENEA

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The Trematodes or Flukes II. Schistosomes

Human Schistosomiasis

Schistosomiasis is today one of the most important human diseases caused by animal parasites. While hookworm disease has gradually been decreasing as a public health problem in most parts of the world, and chloroquine and DDT have suddenly sharply tipped the balance against malaria, schistosomiasis is on the upgrade. In spite of intensive research there is still no easy cure for it and no easy means of control, and extension of irrigation projects and concentration of human populations is increasing its distribution and its intensity. Stoll (1947) estimated that there are 114,000,000 people infected with schistosomes in the world, 46,000,000 of them in the Orient. Wright (1950) thought the number in the Orient, on a conservative estimate, might be no more than two-thirds of Stoll's figure, but it is probable that Stoll's figures for Africa are too low. In lower Egypt, for instance, an incidence of 60 per cent infection was estimated, but more thorough-going diagnosis demonstrated 95 per cent in some localities. Instead of 6,000,000 schistosome infections in Egypt, there are probably more like 10,000,000. Schistosomiasis is undoubtedly one of the principal scourges of that country.

The seriousness of schistosomiasis can be judged by Wright's estimate that infection of 1700 American troops during the recapture of Leyte in 1944 caused the loss of over 300,000 man-days and medical care costs of \$3,000,000, not to mention subsequent veterans' benefits. Hunter et al. (1952) estimated an annual loss of \$3,000,000 in wages and treatment costs in just one of the five endemic areas in Japan (about 90 square miles).

The Parasites. The human schistosomes and most of the other species in mammals belong to the genus *Schistosoma*,* in the family Schistosomatidae. This family shows affinity with strigeids and certain other flukes (see p. 268) in having miracidia with two pairs of flame

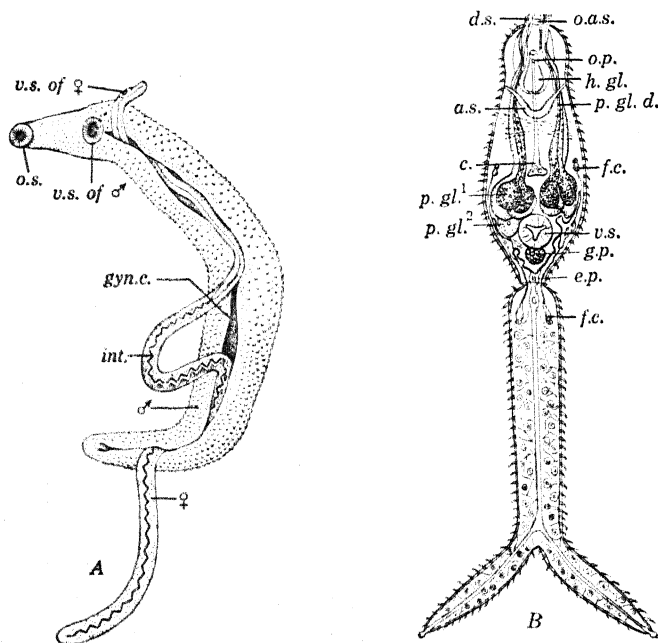


FIG. 65. A, Blood fluke, *Schistosoma haematobium*: male (♂) carrying female (♀) in gynecophoric canal (gyn.c); int., intestine of ♀; o.s., oral sucker of ♂; v.s., ventral sucker. $\times 8$. (Adapted from Looss.) B, cercaria of *S. japonicum*: a.s., anterior sucker; c., cecum; d.s., duct spines; e.p., excretory pore; f.c., flame cells; g.p., genital primordium; h.gl., head gland; o.a.s., orifice of anterior sucker; o.p., oral pore; p.gl.¹, 2 acidophilic penetration glands; p.gl.², 3 basophilic penetration glands; p.gl.d., penetration gland ducts; v.s., ventral sucker. $\times 275$. (Adapted from Faust and Meleney, *Am. J. Hyg.*, Monograph Ser., 1924.)

cells, daughter sporocysts instead of rediae, and cercariae with forked tails, but is peculiar in having separate males and females, which in the genus *Schistosoma* are morphologically quite different. The male, usually about 8 to 16 mm. long, has a cylindrical appearance but is actually flat, with the sides of the body posterior to the ventral sucker rolled ventrally to form a groove or "gynecophoric canal," in which

* The name *Bilharzia* has priority over *Schistosoma*, but before this became known *Schistosoma* was approved by the International Commission on Zoological Nomenclature, which should make it inviolable regardless of later findings. Nevertheless many Europeans (and W.H.O.) prefer *Bilharzia*, honoring the discoverer of the parasites.

the longer and more slender cylindrical female projecting free at each end, but enclosed in the middle, lies safe in the arms of her spouse (Fig. 65A). In most schistosomes they seem to remain permanently wedded and monogamous, the uncoupled females remaining spinsters, but in *Schistosoma mansoni* the union is of more companionate nature. Oddly enough, the female worms do not become sexually mature until they become associated with males, although the males are able to develop quite independently of the females (see Moore et al., 1954).

Both male and female worms are provided with oral and ventral suckers; in the male the ventral sucker is large and powerful. The digestive tract has no pharynx, and the esophagus forks, as usual, just anterior to the ventral sucker, but the forks reunite in the middle portion of the body to be continued as a single tube (Fig. 67). The male worm has several testes just behind the ventral sucker, and it is here that the genital pore opens. The female has an elongated ovary situated in the fork where the intestinal ceca rejoin. Most of the posterior half of the worm is occupied by the yolk glands. Anterior to the ovary is a straight uterus which contains a small number of eggs, 1 to 50 or more in the different species.

Unlike most flukes, the schistosomes do not develop great numbers of eggs all at once, but instead develop them gradually and have only a few in the oviduct at any one time. Schistosomes live for many years.

Life Cycle. The human schistosomes and most of the other species live in small mesenteric or pelvic veins, but one species in cattle, *Schistosoma nasale*, lives in veins in the nasal and pharyngeal mucosa. The female forces her slender body into as small blood vessels as possible, and there deposits her eggs, one at a time. The eggs (Fig. 67) usually retain their position by their spines and by the contraction of the vessels after the body of the parent worm has been withdrawn; aided by histolytic secretions of the embryo inside, they gradually work their way out of the vessels and into the tissues of the walls of the intestine or bladder, and finally into the lumen of these organs, whence they escape with the feces or urine. Some of the eggs, however, are accidentally carried to the liver or lungs where, as in other organs, they set up inflammations. Eventually the irritated tissues become so thickened that most of the eggs are trapped. The eggs of *S. japonicum* take 9 or 10 days to develop mature miracidia while passing through the tissues, and will live for 10 or 12 days longer if not expelled, but many die in the tissues, becoming blackened and calcified. *S. mansoni* eggs remain alive in tissues of experimentally infected mice for 3 to 4 weeks after the parent worms have been killed by drugs.

Cross-fertilization between different species is possible. The sex of

the future adult worms is already determined in the miracidium; of the thousands of cercariae developing from a single miracidium all produce worms of one sex.

Dilution of the feces or urine in water causes the eggs to hatch within a few minutes to several hours or more; in undiluted feces or urine the eggs survive for some time but do not hatch; but in water in cold weather they may survive for several months. The miracidia (Fig. 66A) live for 24 hours or less, and therefore must find a snail

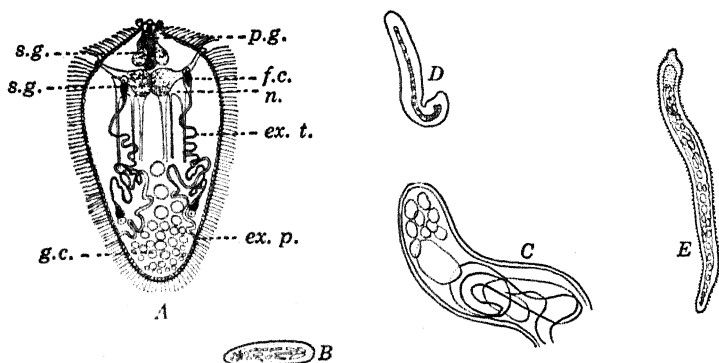


FIG. 66. Stages in life-cycle of schistosomes. A, miracidium of *S. haematobium*. Abbreviations as in Fig. 63A; $\times 300$. (From *Human Helminthology*, by Ernest Carroll Faust, Lea and Febiger, Philadelphia.) B, primary sporocyst 8 days after infection. C, mature primary sporocyst (19 days). D, young daughter sporocyst (19 days). E, mature daughter sporocyst. (B, C, D, and E $\times 35$; after Faust and Hoffman, *Puerto Rico J. Publ. Health Trop. Med.*, 10, 1934.)

of a suitable species within this time. The snails that will serve as intermediate hosts are different for each species of schistosome. When the miracidia come close to a suitable snail they become excited and make a dash for it, burrowing into the tentacles or other parts, much to the irritation of the snail. Many miracidia become mired in the tough tissues of the foot or head; those attacking the soft parts succeed in embedding themselves within a half hour after the attack begins. During penetration the ciliated outer coverings are shed and the miracidia elongate and become tubular sporocysts. These make their way through the viscera to the digestive gland at the innermost extremity of the snail.

In *S. mansoni* the sporocysts reach a length of 1 mm. in about two weeks, and begin to produce daughter sporocysts which burst free from the mother sporocyst. These in turn, reaching a length of 1.5 mm. by 0.09 mm., produce forked-tailed cercariae from germ masses at

their posterior ends. The mature cercariae (Fig. 65B) begin emerging from a birth pore near the anterior end of the sporocyst, which continues to produce them for several months. *S. haematobium* and *S. mansoni* are said to begin shedding cercariae about 4 to 6 weeks after infection under optimum conditions, but in Leyte *S. japonicum* was found to require 11 weeks. A snail infected by a single miracidium of *S. mansoni* was observed by Faust and Hoffman (1934) to discharge an average of 3500 cercariae a day for a long time; in one instance the total progeny of a single miracidium exceeded 200,000.

The cercariae of *haematobium* and *mansoni* have a body about 200 μ long with a tail stem slightly longer and forks about 75 μ long; those of *japonicum* are slightly smaller. They escape from the snail into the water in "puffs," a number at a time. For two or three days the cercariae alternately swim and rest in the water; if they fail to reach a final host in this time they die. If successful they burrow through the skin, using the histolytic and hyaluronidase-bearing secretions of their penetration glands just as the miracidia do. The natives of some parts of Africa where *S. haematobium* occurs realize that infection may result from bathing, but from the nature of the disease they believe that infection takes place by way of the urinary passages, and therefore vainly employ mechanical devices to prevent infection in this manner. Ruminants, because of the neutral or alkaline nature of parts of the stomach, can become infected with schistosomes by drinking cercaria-infected water, but other animals cannot.

Skin penetration requires several minutes and may or may not be accompanied by a prickling sensation and subsequent dermatitis (see p. 293). If ingested with water the cercariae attach themselves to the mucous membranes of the mouth or throat and similarly bore in. They leave their tails behind them, and can be found in the skin for about 18 hours, but eventually they find their way into the blood system and are carried via the heart to the lungs. Young *S. mansoni* accumulate in the lungs on the second and third days; by the sixth day they appear in numbers in the liver, where they are well established by the fifteenth day. Apparently these larvae feed only on the portal blood, but once in the liver they grow rapidly. Migration of this species to the mesenteric veins begins about the twenty-third day, and mating and egg production about the fortieth day.

Species in Man. There are three species of *Schistosoma* which are habitual human parasites of wide distribution—*S. haematobium*, *S. mansoni*, and *S. japonicum*, the first affecting primarily the urinary system, the other two the intestine. *S. haematobium* has large, terminal-spined eggs measuring 115 to 170 μ by 45 to 65 μ (Figs. 57A,

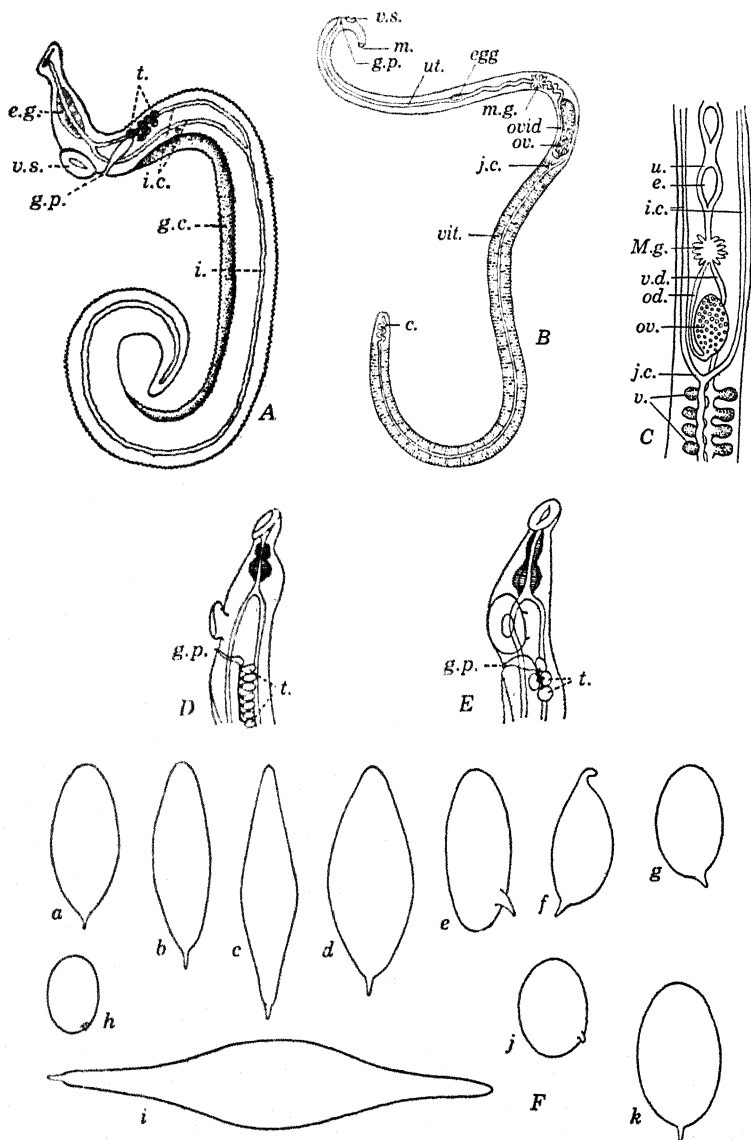


FIG. 67. Schistosome adults and eggs. A, ♂ *S. mansoni*; B, ♀ *S. mansoni*; C, ovarian region of *S. haematobium*; D, anterior end of ♂ *S. japonicum*; E, anterior end of ♂ *S. haematobium*; e., egg; e.g., esophageal glands; g.p., genital pore; g.c., gynecophoric canal; i., intestine; i.c., intestinal ceca; j.c., junction of ceca; M.g., Mehlis' gland; od., oviduct; ov., ovary; t., testes; u., uterus; v., vitellaria; v.d., vitelline duct; v.s., ventral sucker. F, a-k, eggs of various schistosomes: a, *haematobium*; b, *intercalatum*; c, *bovis*; d, *matheei*; e, *mansoni*; f, *rodhaini*; g, *incognitum*; h, *margrebowiei*; i, *spindalis*; j, *japonicum*; k, *indicum*. (Adapted from various authors; F mostly from Schwetz, Baumann, and Fort, *Ann. soc. belge méd. trop.*, 33, 1953.)

67F, a); 4 to 6 testes in the males; the female with the ovary posterior to the middle of the body; 20 to 30 eggs in the uterus; and a tuberculated cuticle. *S. mansoni* has lateral-spined eggs of similar size (Figs. 57B, 67F, a); 8 or 9 testes; the ovary anterior to the middle of the body; only 1 egg in the uterus; and a tuberculated body. *S. japonicum* has smaller and more rounded eggs (70 to 100 μ by 50 to 65 μ) (Figs. 57C, 67F, j), with a rudimentary lateral spine that is often difficult to see; 7 testes; ovary posterior to the middle of the body; 50 or more eggs in the long uterus; and a smooth cuticle. The cercariae of these three species are distinguishable by the number and type of their penetration glands.

S. haematobium and *S. mansoni* are rarely found in nature in animals other than man although *S. mansoni* is sometimes found in monkeys, but both can be reared in a variety of rodents in the laboratory. *S. japonicum*, on the other hand, is a common parasite of cattle, goats, pigs, dogs, and cats among domestic animals and also weasels, meadow mice, and moles in the wild animals. *S. haematobium* is widely distributed in Africa, the Middle East, and part of Portugal; *S. mansoni* over most of Africa and also in South America from Brazil to Venezuela, and in some of the West Indies; and *S. japonicum* in the Far East in Japan, China, some of the Philippine Islands, and Celebes.

The intermediate hosts of these three species belong to three distinct families of snails (see p. 272); those of *S. haematobium* to the family Physidae (or Bulinidae), those of *mansoni* to the family Planorbidae, and those of *japonicum* to the family Hydrobiidae, but only certain species of certain genera of these families are satisfactory hosts. Not only this, but strains of one species may vary in their ability to serve as hosts, and may be good hosts for one strain of a parasite and not another. For example, Files (1951) found that *Australorbis glabratus* from West Indies and Venezuela is more susceptible to strains of *S. mansoni* from the Western Hemisphere than from Egypt, and one strain of this snail from Brazil was found refractory to all strains of *mansoni*. *Planorbis* (*Biomphalaria*) *boissyi* from Egypt is receptive only to Egyptian *mansoni*, but *P. pfeifferi* in Liberia is a good host for *mansoni* from either Egypt or America. Likewise in northern parts of Africa and the Middle East, *S. bovis* of animals develops in *Bulinus truncatus* but not in *B. (or Physopsis) africanus*, whereas in other parts of Africa *S. bovis* develops in *B. africanus* but not in *B. truncatus*. In non-susceptible snails there is a tissue reaction around the invading miracidia within 12 to 24 hours which destroys them in a few days, whereas in good hosts there is no apparent reaction (Brooks, 1953).

The three widespread human schistosomes discussed above are repre-

sentative of groups of schistosomes which some writers, e.g., Schwetz et al. (1954), consider species, but which others, e.g., Amberson and Schwarz (1953), consider subspecies. Related to *S. haematobium* are three other African schistosomes, and one in India, which differ in the shape of their eggs (Fig. 67F,b,c,d, and k) and in their definitive hosts, though all use *Bulinus* or *Physopsis* as intermediate hosts. These are the widely distributed *S. bovis* of cattle, sheep, and goats; *S. mattheei* of sheep in South Africa; *S. intercalatum* of man in Belgian Congo; and *S. indicum* of horses and other animals in India. All of these are intestinal parasites, and even *S. haematobium* is primarily intestinal in monkey hosts. Related to *S. mansoni* is *S. mansoni* var. *rodentorum* of rodents, and *S. rodhaini* of rodents and dogs, which has eggs with a subterminal spine (Fig. 67F,f); both of these, like *mansoni*, develop in planorbid snails. *S. japonicum* has a variety in Formosa which does not parasitize man. A species with eggs suggestive of *japonicum*, *S. margrebowiei* (Fig. 67F,h), has been found in African animals, and similar eggs have been found in man in Congo and South Africa.

In addition to the above-mentioned species, eggs of a pig schistosome in India, *S. incognitum*, were found by the writer in feces believed to be of human origin; these eggs have a subterminal spine (Fig. 67F,g).

SCHISTOSOMA MANSONI. This is an important human parasite in many parts of Africa and tropical America. In lower Egypt, since the development of perennial irrigation, a majority of the predominantly rural population (fellahin) is infected, and in some irrigated districts in Venezuela Scott estimated up to 90 per cent of the males over 10 years of age to be infected. The adult worms have a special predilection for the branches of the inferior mesenteric veins which drain blood primarily from the large intestine and cecal region, but they occasionally get into the urinary system and have the eggs voided with the urine. A healthy, mated female worm deposits a single egg at a time, about three hundred times a day. Mice, hamsters, gerbils, and cotton rats are the best experimental hosts; rats recover too readily, and in other animals either the eggs fail to be produced, or few worms develop. Egg production begins in about 6 to 7½ weeks in experimental animals.

The intermediate hosts, as noted above, belong to the family Planorbidae. In Africa they are species of the genus *Planorbis*, subgenus *Biomphalaria*. The Egyptian species is usually referred to as *P. boissyi*, and that in most other parts of Africa and Madagascar as *P. pfeifferi*, although several other species have been reported as hosts. Amberson and Schwarz consider even *boissyi* and *pfeifferi* to be subspecies of one species, *P. (Biomphalaria) alexandrina*. *P. boissyi* is a snail of ditches

and ponds, whereas *P. pfeifferi* is a riverine species. In South America *Australorbis glabratus* (Fig. 68B), *A. olivaceus*, and *Tropicorbis centimetralis*, and in the West Indies *A. glabratus* and *A. antiquensis*, serve as hosts. Fortunately the North American planorbids fail to serve as hosts with the exception of *Tropicorbis havanensis* of the southern states, and in only a very few of these do the invading miracidia succeed in producing cercariae.*

S. mansoni infections are almost everywhere associated with perennial irrigation, which provides good breeding grounds for the planorbid snails, and brings man into contact with the water. The danger is

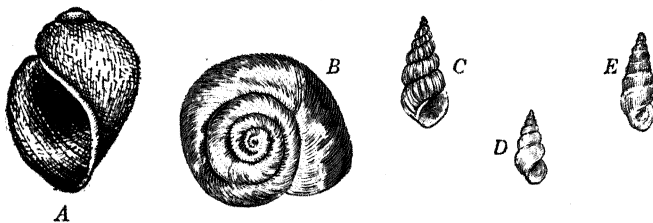


FIG. 68. Intermediate hosts of schistosomes, drawn to scale. A, *Bulinus truncatus*, principal host of *S. haematobium* in Egypt; B, *Australorbis glabratus*, host of *S. mansoni* in tropical America; C, D, and E, *Oncomelania hupensis*, *quadrasi*, and *nosophora*, hosts of *S. japonicum* in China, Philippines, and Japan, respectively. All $\times 2$.

intensified by the Moslem custom of washing themselves after defecation; as Khali pointed out, a habit directed towards personal cleanliness has become a dangerous contributor to disease. An interesting situation exists in Egypt where both *mansoni* and *haematobium* are prevalent in the delta, but only *haematobium* in Upper Egypt, although both species are again prevalent in Sudan. Helmy showed that this was because *Planorbis boissyi* is a quiet-water, surface-feeding snail, and although washed down the Nile from the Sudan it fails to find landing places until the current becomes very reduced, whereas *Bulinus truncatus*, the snail host of *S. haematobium*, settles to the bottom and crawls out. The difference is strikingly demonstrated by putting *Planorbis* and *Bulinus* in a glass of water and emptying it—*Planorbis* is poured out but *Bulinus* clings to the glass.

SCHISTOSOMA HAEMATOBIMUM. This schistosome is very prevalent in many parts of Africa, Madagascar, and southwestern Asia, and a few

* A W.H.O. study group placed all of the above *S. mansoni* intermediate hosts in the single genus *Biomphalaria*, and also placed the snail hosts of *S. haematobium* (*Bulinus*, *Physopsis* and *Pyrgophysa*) in a subfamily (Bulininae) of the same family, Planorbidae. (W.H.O. Tech. Rept. Series, 90, 1954.)

cases have been reported in India. It is especially prevalent in Egypt and affects 60 to 95 per cent of the fellahin in lower Egypt, where perennial canal irrigation is practiced. It is becoming commoner in Iraq and parts of Syria, Palestine, and Iran as irrigation systems are developed. In Bagdad 25 per cent of the males (60 per cent in some parts of the city) are infected, and in Basrah 33 per cent. In some rural areas 75 to 80 per cent of the males are infected; the females usually show a somewhat lower incidence. Throughout the greater part of Africa, both north and south of the Sahara, *S. haematobium* infections are prevalent wherever local conditions are favorable for the snail vectors and wherever people bathe or work in the water or drink it unfiltered. Kuntz (1952) found open ablution basins in mosques in Yemen to be a breeding ground for snails, and the main source of schistosome infections.

The adult worms live in the pelvic veins of the vesical plexus, and the females normally deposit their eggs in the walls of the urinary bladder, urethra, or ureters, through which the eggs work their way to be voided with the urine; a few eggs, however, often get into the feces also. As with other species, eggs are often swept back to the liver and on to the lungs or other organs. *S. haematobium* can be reared in hamsters experimentally, less readily in mice, and not at all in rats or rabbits.

The intermediate hosts, except in Portugal where a planorbid, *Planorbium corneum metidjensis*, has been incriminated, belong to the family Physidae or Bulinidae—*Bulinus*, *Physopsis*, and *Pyrgophysa*. (But see footnote, p. 285.) Some consider all of these as merely subgenera of *Bulinus*. In North Africa, the Mediterranean area, southwestern Asia, the East African highlands, and South Africa, the intermediate host is *Bulinus truncatus* (Fig. 68A) or closely related forms. These are snails of moderately warm countries, but not adapted to the heat of low-lying countries in equatorial Africa, where *Physopsis africana* and closely related forms are the hosts. Both these species occur together in many parts of Africa, but only *P. africana* in tropical Central Africa and the Guinea Coast. In the island of Mauritius *Pyrgophysa forskalii* is the host. These same snails also serve as hosts for the other African schistosomes with terminal-spined eggs.

As noted on p. 284, in Belgian Congo another schistosome with terminal-spined eggs, *S. intercalatum*, is found in man. Like *S. haematobium*, it uses *Physopsis* as an intermediate host, but it is an intestinal, not a urinary, species.

SCHISTOSOMA JAPONICUM. This species, as noted above, occurs naturally in a great variety of reservoir hosts in many parts of the Orient.

The adult worms live mainly in branches of the superior mesenteric veins; the eggs, up to 3500 a day, are deposited in the walls of the intestine and make their way into the lumen until, as in other species, the wall becomes too thick and the host reaction too great. Not infrequently eggs become imbedded in the appendix also, and may cause appendicitis. More frequently than in the other species the eggs, which are laid in clusters, are swept back into the liver, and often on to the lungs.

The intermediate hosts of *S. japonicum* are small, operculated, amphibious snails of the genus *Oncomelania* (family *Amnicolidae*) (Fig. 68C-E). In Japan the host is *O. nosophora*, a smooth-shelled form; in China it is the rib-shelled *O. hupensis*, and perhaps one or two related species; in the Philippines it is *O. quadrasi*, with a smooth, pointed shell; and in Formosa it is *O. formosana*, but this species will not allow development of *S. japonicum* from Japan. The nearest relative of *Oncomelania* in the United States is *Pomatiopsis* (see p. 300 and Fig. 70C), which is a host for *Paragonimus*. This snail can sometimes produce cercariae of *S. japonicum* but is not a good host.

The snails of this group are only 7 to 10 mm. long with high-spired shells. The young snails live in water but when mature they are amphibious and live in damp places at the edges of water and are commonly found climbing on vegetation, mud, or rocks along irrigation ditches and edges of ponds and streams, especially where the water or soil is enriched with humus or night soil, for they feed on filth. They are frequently submerged with rising or disturbed water and are carried from dirty village ditches to rice fields. While submerged they are attacked by the miracidia, which habitually swim near the surface of the water. In Japan and China irrigation ditches are by far the most important locations for the snails, rice fields less so, but in the Philippines, where agriculture is less highly developed, *O. quadrasi* occurs mainly in small, slow-flowing streams clogged with vegetation.

In northern areas the snails lay their eggs singly in the spring, patting mud or debris on them so that they are hard to detect. The snails get infected in the summer, hibernate in winter, and shed cercariae the following spring. Farther south there are at least two broods a year, and cercaria production is more or less continuous.

Pathology. The diseases produced by various schistosomes are similar in many respects but differ in details. In previously uninfected cases there are three distinct stages of the disease: (1) the period of migration and development to maturity of the young worms; (2) the period of early egg production, when the eggs readily escape to the lumen of the intestine or bladder; and (3) the period of late egg pro-

duction when the eggs tend to be trapped in the tissues. Of course where there are constant reinfections these distinct stages are not recognizable.

During the pre-egg stage the worms are carried to the lungs, then migrate to the liver, and after 3 weeks or more undertake the last lap of their journey to the mesenteric veins. The first symptoms, if there has been heavy exposure to cercariae, is an irritating bronchial cough lasting a few days. After 2 or 3 weeks there is an itching rash, local dermatitis, fever, aches, and other general toxic symptoms of allergic nature, including eosinophilia.

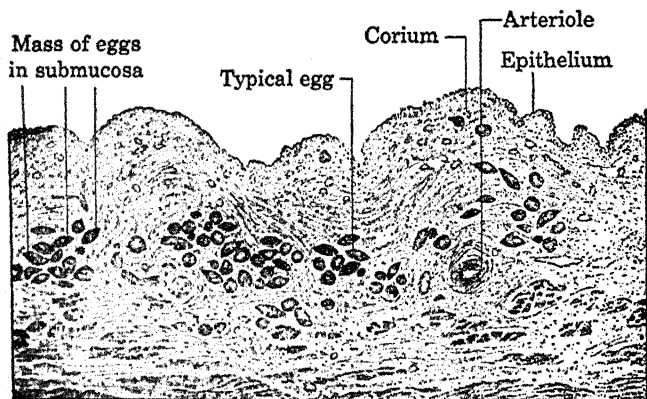


FIG. 69. Section of wall of urinary bladder showing eggs of *Schistosoma haematobium*. (After Brumpt, *Nouveau traité méd.*, 5, 1922.)

During the stage of early egg production, which may last one month to a year, the intestinal species produce blood and mucus in the stools, diarrhea, abdominal pain, and slight liver tenderness, whereas *S. haematobium* produces few symptoms except blood in the urine, often only in the last few drops, and sometimes some irritation from urinating, depending on the severity of the infection.

Gradually, as the tissues become sensitized to the eggs passing through the tissues, and tissue reactions cause the walls of the intestine, bladder, and urinary passages to become thickened and inflamed, trapping large numbers of the eggs, the symptoms of the third stage come on. In the intestinal forms there is recurring diarrhea or dysentery, increasing abdominal pain, and enlargement of liver and spleen. As the disease progresses the liver eventually recedes and becomes contracted and cirrhotic, but the spleen continues to enlarge, the abdomen becomes bloated while the rest of the body is pitifully anemic and emaciated, and abdominal pain may become very great. In *haemato-*

bium infections bloody urine continues with increasing pain on urination, often with constrictions of the urinary passages, and eventually inability of the bladder to contract. Fistulas and even malignant tumors may develop, involving the bladder, prostate, or penis. Usually, however, this infection causes less serious symptoms than does *S. mansoni*. One side effect of the disease is a high incidence of urinary typhoid carriers.

In light cases there may be no noticeable symptoms at all except blood in the stools or urine, or there may be only general symptoms such as loss of appetite, weakness, aches, etc. On the other hand, in severe infections there may be a number of serious complications, particularly from eggs being deposited in arterioles in the lungs, causing what is variously called cardio-pulmonary schistosomiasis, "cor pulmonale," or "ayerza disease." Inability of the blood to pass the clogged vessels in the lungs may lead to cyanosis (blueness from inadequate aeration of the blood), congestive heart failure, aneurisms (blow-outs) of the pulmonary artery or other vessels. In South Africa, *S. haematobium* eggs are found in the lungs of people dying of lung diseases twice as frequently as in those dying of other complaints. There is some evidence that "Egyptian splenomegaly" or Banti's disease, characterized by huge spleen enlargement, edema, and anemia, may also be a manifestation of schistosomiasis.

Lesions in other parts of the body (ectopic lesions) result from aggregates of tubercles forming around eggs which have escaped and have been carried to distant parts of the body; they vary in size from pinhead lesions in the conjunctiva to lesions the size of an orange in the brain. In *S. japonicum* infections a significant proportion occur in the brain, probably because, according to Faust, the vertebral veins provide a natural channel from the portal and caval veins.

Immunity. Little is known about development of immunity to schistosomiasis by man, but experimental animals develop immunity (see Vogel and Minning, 1953; Meleney and Moore, 1954), and there can be no doubt that man does too. Presumably all the manifestations of immunity discussed on pp. 23-24 come into play, particularly interference with reproduction and resistance to reinfection; if this were not so, people constantly exposed in places like Egypt would soon succumb. There is also little doubt that the nutritional status of a community, and of individuals in the community, has as much to do with the severity of the disease as does exposure to it—in the writer's opinion probably even more.

Diagnosis. In early or acute cases, after the worms begin ovipositing, diagnosis of urinary schistosomiasis can be made by finding the

eggs in sedimented or centrifuged urine; if scanty, addition of water to the sediment will cause the eggs to hatch in 5 to 10 minutes, and the swimming miracidia can be seen with the naked eye or by projection on a screen. Exercising before urinating increases the number of eggs in the urine. In stages of early egg production in *mansoni* and *japonicum* infections the modified Telemann technique (see p. 255) can be used for stool examination; if scanty, the eggs can be concentrated by repeated sedimentation or centrifuging in 0.5 per cent glycerin water, after which the sediment can be resuspended in water and swimming miracidia observed after 10 or 15 minutes.

In old chronic cases examination of urine or feces is unreliable since so many eggs become encapsulated in the tissues and do not escape regularly. Those that do are often dead or blackened, or surrounded by a fuzzy coat of cells. In these circumstances rectal scraping gives a much larger number of positives than examination of excreta for eggs, even in *haematobium* infections, where only a minority of the eggs get into the rectum. In a survey in Egypt Weir et al. (1952) found 60 per cent infection by examination of urine sediment for eggs, but by the projection of miracidia method found 31 per cent of the negatives to be positive, and by the rectal scraping method 83 per cent of the negatives were positive; by all three methods combined the incidence was 95 per cent. Immunological tests are also useful in chronic cases, using antigens prepared from cercariae; skin tests, complement fixation, and formation of a precipitate around schistosome cercariae all have their uses. Complement fixation and precipitin reactions are demonstrable within 2 or 3 weeks, skin reactions after 4 to 6 weeks. In a survey in Puerto Rico by Morales et al. (1950) both skin test and biopsy (rectal scraping) proved superior to stool examination, but any one method may miss cases positive by the others. The skin test is easiest to perform and therefore to be preferred in a survey.

Treatment. Tartar emetic (sodium antimony tartrate) and other trivalent antimony compounds, particularly Anthiomaline and Fuadin, have specific effects in schistosomiasis. These drugs cause degenerative changes in the adult worms, especially affecting the reproductive organs. The injured worms lose their hold and are swept into the liver. The drugs do not kill the eggs, but if reproduction of the parent worms is stopped, there will be only dead and blackened eggs in the tissues after about 3 weeks.

Tartar emetic is cheap and effective, but must be given intravenously over a period of about 4 weeks, and it is toxic. Fuadin can be given into the muscles but is more effective intravenously; it is expensive and somewhat less effective but less toxic. Anthiomaline is similar to

Fuadin but less expensive and also less efficient. None of these drugs are as effective against *S. japonicum* as against the other species. Pentavalent antimony compounds are comparatively ineffective. To overcome the long time required for cure, attempts have been made to intensify and shorten the treatment, using courses extending 2 to 10 days, with some success (see Alves and Blair, 1946), but also some danger. Recently a sulfur analog of tartar emetic (TWSb) was reported by Friedheim et al. to be very effective in treatment, and much less toxic than tartar emetic (*Am. Soc. Trop. Med. Hyg.*, Abstracts of Papers, Third Annual Meeting, November 1954).

There is one drug, Miracil D (Nilodin), which is effective against schistosomes when given by mouth. This would be of tremendous advantage if it were not that the drug produces such unpleasant (though not dangerous) toxic symptoms as nausea, vomiting, mental depression, and pains, so severe that many patients prefer their disease. This drug is most effective against *S. haematobium* infections and no good against *S. japonicum*.

In advanced cases where the rectum or urinary organs have been severely damaged, and in all cases of splenomegaly, surgical treatment is necessary.

Prevention and Control. Ultimate control of schistosomiasis resolves itself into destroying or eliminating the snails that serve as intermediate hosts. In the case of *S. mansoni* and *S. haematobium*, in which there are no reservoir hosts, control might also be accomplished by environmental sanitation and prevention of pollution, but any appreciable progress in that direction is not likely to occur in the foreseeable future in most schistosomiasis countries. In the Orient, two to five people have to live off one acre of land, and the use of night soil (human excreta) is necessary to existence. In countries with low rainfall the same irrigation water has to be used for all purposes without purification—swimming, washing clothes, ablutions, drinking, and irrigation.

Copper sulfate, found by the writer (1920) to be destructive to snails, has been the only really effective and practically feasible chemical for control of snails until recent years; enormous amounts of it have been used in Egypt and other parts of Africa. It has the disadvantage that it is quickly rendered non-toxic to snails by combination with alkalis and organic matter, and has no residual effect. Under some circumstances a mixture of the slowly soluble copper carbonate with copper sulfate increases effectiveness.

Intensive search in the last few years has brought to light several other groups of chemicals which show promise. The pentachloro-

phenols are one, of which the sodium salt (Santobrite) seems best. This was found by Hunter et al. (1952) to be so effective against the amphibious snail hosts of *S. japonicum* that not only control, but ultimate elimination, may be possible by spring and fall sprayings of all irrigation ditches—in the fall to kill snails that become infected during the summer and will shed cercariae in the spring, and in spring to kill infected snails before rice planting begins. Against the aquatic Egyptian snails Kuntz and Wells (1951) found a certain dinitrophenol to be lethal at 3 to 5 p.p.m., to remain effective for 2 to 4 weeks in quiet water, and to kill the eggs as well as the snails. Certain mercuric compounds were shown by workers at the National Institutes of Health to be the most effective molluscicides of all in laboratory tests, but field tests have not yet been made. All molluscicides rapidly increase in effectiveness with temperature.

Halawani has called attention to the fact that while complete eradication of snail hosts in Egypt is at present not feasible, very marked reduction in human exposure to infection could be obtained by treating local areas—villages, bridge crossings, washing places, etc.—where the snails are most exposed to miracidia and man most exposed to cercariae. Objection has been raised that snails would quickly invade from untreated parts of ditches, but in Nigeria stretches of streams 1½ to 3 miles long, freed of snails, remained free for 10 to 11 months.

Additional control methods, locally applicable, consist of paving or clearing vegetation from ditches, use of natural enemies of snails, and wholesale treatment. The last might be feasible if a drug could be found which would prevent passage of viable eggs. Attempts are being made in Brazil to utilize pathogenic bacteria as natural enemies. A snail, *Marisa*, avidly devours eggs of *Australorbis*, and certain leeches are destructive to it.

For personal protection against cercariae, e.g., in military operations, Hunter et al. (1952), in tests against schistosome dermatitis, found copper oleate ointment to be effective for 6 to 8 hours, and ointments containing dibutyl or dimethyl phthalate or benzyl benzoate for 4 to 6 hours. A dimethyl phthalate cream has been used in Australia against schistosome dermatitis. Clothing impregnated with mixtures of these chemicals, with a detergent added as an emulsifier, is protective even after several soap-and-water washings. Some protection is obtained by carefully wiping the skin after immersion in infected waters, although if given time the cercariae can penetrate while submerged. Protection against cercariae in drinking water and in unfiltered urban water supplies is possible by impounding the water for 48 to 60 hours,

or by treatment with enough chlorine to give a residual of 0.5 p.p.m. for 15 minutes or 0.1 p.p.m. for 30 minutes.

Schistosome Dermatitis (Swimmer's Itch)

The penetration of the skin by the cercariae of human schistosomes usually causes a prickling sensation and may or may not cause an itching rash or papules; these skin effects are undoubtedly conditioned by the extent of prior invasion and sensitization or immunity.

As Cort demonstrated in 1928, certain species of "foreign" cercariae, incapable of infecting man, cause a severe dermatitis or "swimmer's itch" when they penetrate the skin of bathers or waders who have become sensitized by repeated exposure. This condition annoys vacationers on sunny bathing beaches in northern United States and southern Canada, from New England and Quebec to Manitoba and Oregon. In the north central states *Cercaria stagnicola* is the most important since its host, *Stagnicola emarginata*, inhabits the same waters as the human bathers, and the cercaria, like the bathers, swarm near the surface in shallow water on warm, sunny days. McMullen and Beaver (1945) believe that the snails acquire their infections mainly from migrating ducks in the fall when the beaches are otherwise deserted. Swimmer's itch also affects clam diggers and sea bathers on the North Atlantic coast, bathing beauties in Florida, naturalists on rocky shores of southern California and Mexico, fishermen in San Salvador, carp breeders in Germany, rice growers in Japan and Malaya, and lake bathers in Australia and New Zealand.

It may be expected that wherever suitable snail hosts are present in abundance, and birds or other definitive hosts congregate in sufficient numbers and for a long enough time to infect them, and human beings then repeatedly come in contact with the water, swimmer's itch is likely to be a nuisance. Most of the known fresh-water itch-producers, which are cercariae with eye spots belonging to the *Cercaria ocellata* group, develop into species of *Trichobilharzia* in ducks; two others develop into species of *Gigantobilharzia* in passerine birds; one into *Schistosomium douthitti* in rodents; and one into *Schistosoma spindalis* of cattle and goats (see Cort, 1950). One marine form occurring in Rhode Island and Long Island and in Hawaii develops into a *Microbilharzia* of shore birds (see Chu and Cutress, 1954). The marine forms from Florida and California are thus far of unknown parentage.

Although some cercariae penetrate the skin under water, the annoyance can be much reduced by wiping the skin dry immediately after leaving the water. Children getting alternately wet and dry in shallow water are affected worst. The dermatitis begins with a prickly sensa-

tion followed by the development of extremely itchy papules, which sometimes become pustular and may be accompanied by considerable swelling. Some individuals are much more severely affected than others and may lose much sleep and even be prostrated. It usually takes about a week for the condition to subside. In previously unexposed laboratory mammals, and probably in man, bird schistosomes after skin penetration migrate to the lungs and may produce pulmonary hemorrhages, but they fail to go on to the liver (Olivier, 1949). It is only after sensitization that the cercariae are trapped in the skin by tissue reactions. They soon die in the skin and cause allergic irritation.

After penetration soothing and/or anti-histaminic applications are said to be helpful. The dermatitis can be effectively controlled in small bodies of water by the use of copper salts to kill the snails. McMullen and Brackett recommend copper sulfate for shallow water, and a 2 to 1 mixture of copper sulfate and copper carbonate for water over 2 ft. in depth, at the rate of 3 lb. of the mixture per 10,000 sq. ft. of bottom. In larger lakes attention to water currents is necessary.

Animal Schistosomes

Cattle, sheep, and goats are severely affected by several species of schistosomes in Africa and Asia, the most important being *S. bovis* in Africa, Southern Europe, and Asia; the nearly related *S. mattheei* of South Africa; *S. spindale* in India, South Africa, and Sumatra; and *S. nasale* (possibly = *S. spindale*) in India. *S. indicum*, confined to India, also affects these animals, but more frequently horses and camels; and *S. incognitum*, the eggs of which the writer first described from feces believed to be human, occurs in pigs and dogs in India. In the Orient many animals are parasitized by *S. japonicum*. These various species are distinguishable by their eggs (Fig. 67F). In Africa the intermediate hosts are the same as those of *S. haematobium*, or related species of the family Physidae (Bulinidae), whereas the commonest host in India is a planorbid, *Indoplanorbis exustus*. In addition to these members of the genus *Schistosoma* there are several species of *Ornithobilharzia* which live in cattle, elephants, and other animals.

S. nasale causes a "snoring" disease of cattle; it localizes in the nose and produces cauliflower-like growths on the nasal septum. All the other species have their eggs voided with the feces, though sometimes with the urine as well. These parasites cause lowered vitality, especially, no doubt, in poorly nourished animals, and cause economic loss from unsalability of the liver.

Ducks sometimes suffer from various species of the subfamily Bilharziellinae, which differ from the typical schistosomes in having both sexes alike in size and form. Cercariae of some of these, as well as those of *S. spindale*, cause swimmer's itch in man.

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The Trematodes or Flukes

III. Other Trematodes

Lung Flukes (*Paragonimus*)

The lungs of various mammals, including man, carnivores, rats, pigs, and opossums, may be infected with flukes of the genus *Paragonimus*, belonging to the family Troglotrematidae. The members of this family are rather small egg-shaped flukes with a spiny cuticle and with the large testes situated side by side behind the ovary. Besides *Paragonimus* the family includes *Nanophyetus salmincola*, the salmon-poisoning fluke (see p. 320), and a fluke that lives in cutaneous cysts in birds, *Collyriclum faba*.

Species. Opinion is divided as to the number of species of lung flukes. In the adults differences occur principally in the body spines and in the size of the eggs, but these are both variable characters. The first form described was *Paragonimus westermanni* from Bengal tigers, whereas the first human specimen, from Formosa, was named *P. ringeri*. A North American form, normally a parasite of mink, has been named *P. kellicotti*. Investigations of the life cycles have demonstrated differences in both the morphology and the behavior of the different developmental stages, not only between Korean and American forms, but also between various Oriental forms. A species parasitizing rats was found by Chen near Canton which would not develop in carnivores, pigs, or monkeys, and another species, *P. ohirai*, occurs in pigs and sometimes dogs in Japan; the latter species is difficult to distinguish from *P. westermanni* in the adult stage, but the larval stages are different. It is still uncertain whether *P. ringeri* and *P. westermanni* are distinct species. The North American form described by Ameel (1934) is a rather common parasite of mink in Michigan, and infected crayfish have been found over a large part of the United States. Since infection is caused by eating raw crabs or crayfish, which serve as second

intermediate hosts, human infection is sporadic in most places but is endemic in many parts of the Orient, especially in Korea, Japan, the Philippines, and parts of Indo-China. In some localities 40 to 50 per cent of the population are infected. Human infections have also been reported from New Guinea, Indonesia, India, tropical Africa, Ecuador, and the United States.

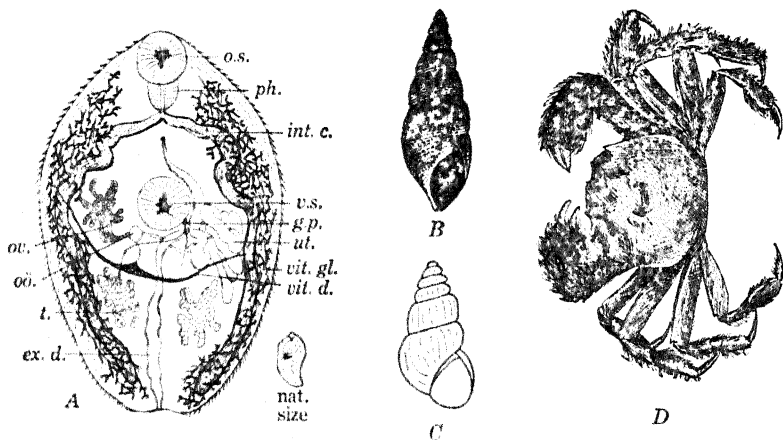


FIG. 70. Lung fluke, *Paragonimus westermani*, and first and second intermediate hosts. A, adult fluke; g.p., genital pore; oo., oötype; other abbreviations as in Fig. 58 on page 261. B, *Semisulcospira libertina*, snail host in Japan and Korea. C, *Pomatiopsis lapidaria*, host of *P. kellicotti* in the United States. D, *Eriocheir japonicus*, a common second intermediate host in Japan. (Adapted from various authors.)

The adult flukes are reddish brown, thick, and egg-shaped, about 8 to 12 mm. long and 4 to 6 mm. in diameter. The cuticle is clothed with minute simple or toothed spines. The arrangement of the organs can be seen from Fig. 70A.

Life Cycle. The adults live normally in the lungs where, shortly after they have arrived, the host forms cyst-like pockets around them, which rupture and liberate the eggs into the bronchial tubes, to be excreted with sputum. These cysts are usually about the size of filberts or larger, and contain commonly two but sometimes as many as six worms, together with infiltrated cells and numerous eggs in a rust-brown semifluid mass. Many of the eggs escape into the tissue, giving it a reddish peppered appearance and causing small tubercle-like abscesses. In some cases the worms apparently get on the wrong track in the body and end up in such places as the spleen, liver, brain, urinary system, intestinal wall, eye, or muscles. In one case more than a hundred mature parasites were found in a muscular abscess.

The eggs (Fig. 57D) are yellowish brown, 80 to 118 μ in length by 48 to 60 μ in diameter; they are commonly found in the feces as the result of being swallowed. Miracidia develop in the eggs slowly after they leave the body, requiring at least 3 weeks, during which time the eggs must be kept moist.

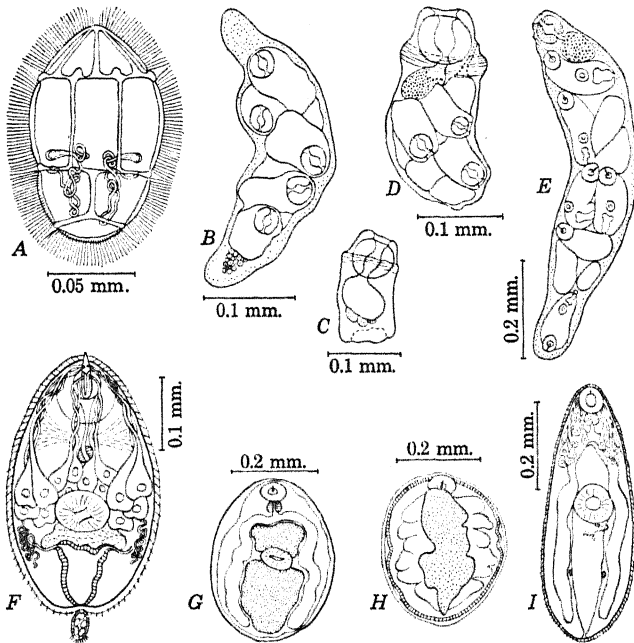


FIG. 71. Stages in life cycle of *Paragonimus kellicotti*. A, miracidium, showing ciliated epidermal plates and flame cells; B, mature sporocyst containing first-generation rediae; C, young first-generation redia; D, mature first-generation redia containing second-generation rediae; E, mature second-generation redia containing cercariae; F, microcercous cercaria; G, young encysted metacercaria, 5 weeks old; H, mature encysted cercaria; I, excysted cercaria, showing excystation glands and beginning of genital organs (refractile granules in large excretory bladder not shown). (After Ameel, *Am. J. Hyg.*, 19, 1934.)

The life cycle of the worm was established in part by several Japanese workers from 1918 to 1921, but the first complete account of the life cycle and of the developmental stages (Fig. 71) was given by Ameel (1934), who studied the American form in Michigan. The miracidia hatch in water and enter suitable snail hosts by burrowing. In the Orient the snail hosts are species of the family Thiariidae (see p. 272), principally *Semisulcospira libertina* (Fig. 70B), *S. amurensis*, and *Thiara granifera* (introduced into Florida), all once included in the

genus *Melania*. Small amphibious snails of the family Hydrobiidae (see p. 272) may also be involved. *Syncera lutea* is a host of a *Paragonimus* found in rats in China, and *Pomatiopsis lapidaria* (Fig. 70C) is the host of *P. kellicotti* in Michigan.

In the snails the miracidia change into sac-like sporocysts, which produce about twelve first-generation rediae; they in turn produce a similar number of second-generation rediae. The last produce 20 or 30 fully developed cercariae. These are 175 to 240 μ long, have a small knob-like tail, spiny cuticle, a stylet, and 14 penetration glands; these cercariae appear 78 days or more after infection of the snail. The cercariae do not swim, but creep in a leech-like manner or float with the current. Those of the American species pierce the cuticle of the crayfish, which is the next host in the series, at vulnerable points and make their way invariably to the heart and pericardium where they become encysted and gradually develop into mature infective metacercariae, a process which takes 6 weeks or more. In China and Japan various species of fresh-water crabs serve as second intermediate hosts, and in Korea a crayfish is involved. The Oriental forms do not choose the cardiac region but encyst principally in the gills and the muscles of the body and legs, and sometimes in the liver. The metacercarial cysts (Fig. 71H) are nearly round, 0.5 mm. or less in diameter. The enclosed spiny metacercariae lie straight, unlike most encysted forms, and are characterized by the large excretory vesicle filled with refractile granules, with large convoluted intestinal ceca on either side.

Second Intermediate Hosts. Crabs of the genera *Eriocheir* and *Potamon* are commonly infected in Japan. *Eriocheir japonicus* (Fig. 70D) has the highest incidence of infection in Japan—over 90 per cent in some areas in late summer. This crab inhabits rice fields near the sea and small inland streams, and is extensively used as food. The species of *Potamon* are coarse-shelled crabs which abound in shallow water of mountain streams in Japan, Formosa, and the Philippines. Another frequently infected crab is *Sesarma*, but this is not an edible form. In the United States probably all the species of *Cambarus* serve as hosts; small sluggish streams, 20 to 30 ft. or less in width, have been found to contain the greatest numbers of infected crayfish, whereas large streams contain few if any.

Infection usually results from eating the infected crabs or crayfish without cooking. In parts of China and the Philippines, as well as in Japan and Korea, crabs are eaten raw with salt or dunked in wine or vinegar. In some parts of Japan the crabs are not eaten raw but are

crushed on a chopping block, which is subsequently used for preparation of other foods that become contaminated by the liberated metacercariae. In some localities the people drink raw juice of crabs or crayfish to reduce fever. Possibly water containing cysts liberated from the gills of dead crabs may also be a source of infection, for such cysts live for some weeks.

Development in Final Host. When the young flukes are freed from their cysts in the duodenum of their final hosts, they bore through the walls of the intestine, wander about in the abdominal cavity for some time, then go through the diaphragm to the pleural cavity, into the lungs, and finally to the bronchioles, where they remain and grow to maturity in the cysts formed by the host's lung tissue. In a normal host they may reach the pleural cavity in about 4 days and enter the lungs after about 2 weeks, but Ameel found that in white rats they may still be loitering in the abdominal cavity, bereft of ambition or purpose in life, after more than 8 months. Man is probably not the normal host for *Paragonimus*; the frequency with which the worms get lost and find themselves in abnormal localities may be correlated with this fact (see p. 26). The worms in the lungs are long-lived, persisting for at least several years. A German who had become infected in America while enjoying the delicacies provided by a Chinese cook claimed to have had symptoms of lung infection for 10 years before his trouble was diagnosed, and it was not until 13 years later that his symptoms finally disappeared.

The effects produced by *Paragonimus* infection are usually not serious, although they are suggestive of tuberculosis. The most constant symptoms are a cough, which is usually intermittent, blood-stained sputum, mild anemia, slight fever, and weariness. Only rarely are patients incapacitated for work. Positive diagnosis can be made by finding the eggs in the sputum or the feces, where they can be found in about two-thirds of the cases by the AMS III technique (see p. 255). Skin tests using extracts of powdered worms as antigen are also said to be very reliable.

Treatment and Prevention. No reliable treatment is known, but emetine hydrochloride together with sulfonamides is sometimes effective. Prevention of infection consists either in destruction of the snails that serve as intermediate hosts (see pp. 291-292); abstaining from the use of raw crabs or crayfish for food, or of their juices as home remedies; care not to contaminate utensils, etc., during culinary operations on the crabs; and avoidance of use of water for drinking which may possibly contain detached cysts.

Liver Flukes

FASCIOLIDAE

The liver and bile ducts of man and domestic animals are inhabited by flukes of the families Fasciolidae, Dicrocoeliidae, and Opisthorchiidae.

The Fasciolidae include several species of the genera *Fasciola* and *Fascioloides* which are very important liver parasites of cattle, sheep, and goats; *Fasciola* is not infrequently parasitic in man. This family also includes *Fasciolopsis buski* (see p. 314), an important intestinal fluke of man and pigs. The Fasciolidae are large leaf-like flukes with branched reproductive organs and usually branched ceca also, with a small coiled uterus lying entirely in front of the sex glands. The eggs are very large; the cercariae (Fig. 63J), which have long simple tails, encyst on water vegetation.

Fasciola hepatica is 25 to 30 mm. long, with a small anterior cone, as in other members of this genus, giving it a shouldered appearance. The general arrangement of the organs can be seen from Fig. 72. It is found in cattle, sheep, and goats in nearly all parts of the world and has been found in the livers of many other animals including marsupials, rodents, rabbits, pigs, horses, carnivores, and primates. Olsen in 1948 called attention to the importance of rabbits as reservoirs of infection. In many parts of Africa and the Orient, including Hawaii, *F. hepatica* is replaced by a similar but even larger species, *F. gigantica*. Another related form, *Fascioloides magna*, which lacks the anterior cone, is primarily a parasite of deer in North America but also frequently infects cattle; in cattle it commonly becomes encapsulated in the liver tissue, whence its eggs fail to escape from the host. Sheep may be severely affected by this species (Swales, 1935). Deer are usually *not* parasitized by *F. hepatica*.

In cattle, sheep, and goats these liver flukes cause very considerable damage, especially in young animals, which become unthrifty and emaciated and under adverse conditions die. Olsen estimates that on the Gulf Coast alone there is an annual loss of 44 tons of condemned livers (23 per cent) and 58 tons of meat, to say nothing of mortality, particularly among calves, reduction in milk production, and curtailed breeding. In India, according to Bhalerao, *F. gigantica* causes more damage to cattle than any bacterial or virus disease.

Human infection is not infrequent in some countries. Watercress is one of the commonest means of infection, but home-grown watercress is seldom exposed to *Fasciola* cercariae. In Cuba Kourí (1948) reported

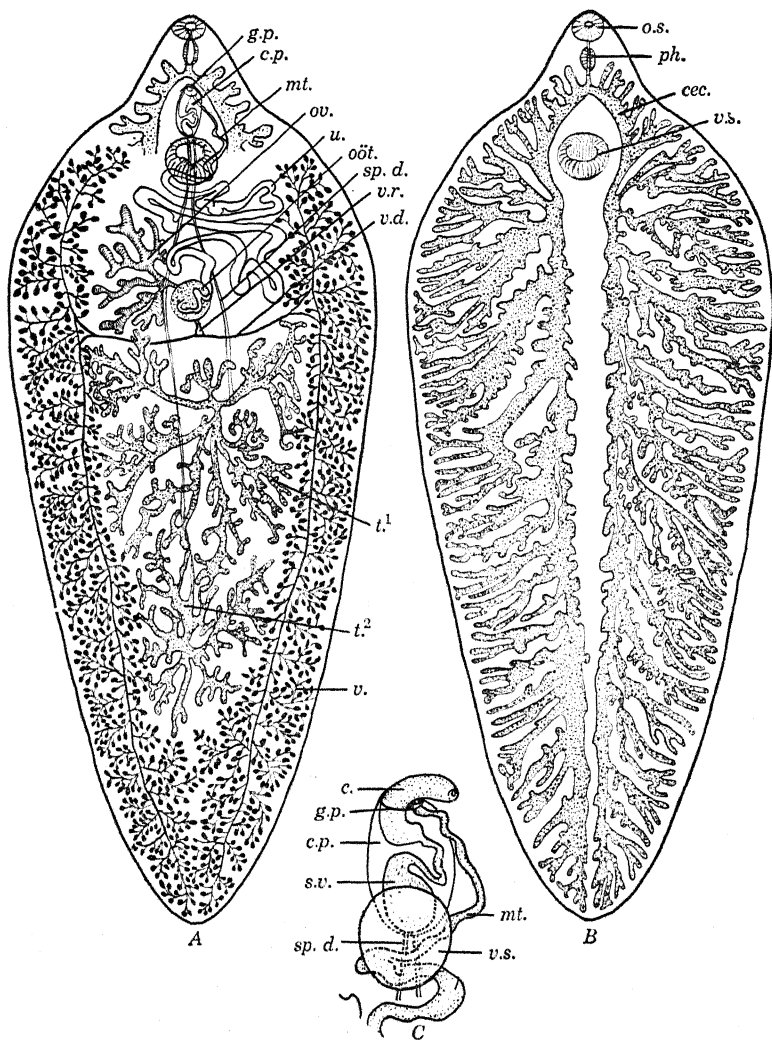


FIG. 72. *Fasciola hepatica*. A, showing reproductive systems only; B, showing digestive system only; C, cirrus pouch region. Abbreviations: c., cirrus; cec., cecum; mt., metraterm; oöt., oötype; sp.d., sperm duct; t^1 , anterior testes; t^2 , posterior testis; v.d., vitelline duct; v.r., vitelline reservoir; other abbreviations as in Fig. 58. (Adapted from Leuckart's chart.)

human fascioliasis to be quite common, particularly in certain provinces, in some years actually reaching epidemic proportions. Serious symptoms appear, involving the liver, gall bladder, alimentary canal, and nervous system. During the period of invasion there is a syndrome of fever and eosinophilia. A fatal human case of *F. gigantica* infection, due to obstruction of biliary ducts, was reported in Hawaii.

Eggs of *Fasciola* develop after leaving the host and hatch in about 2 weeks. The miracidia develop in snails of the genus *Lymnaea* (Fig. 63) or closely related genera (*Stagnicola*, *Fossaria*, *Galba*, *Pseudosuccinea*) and go through a sporocyst and two redia stages before the cercariae are produced. The latter leave the snail in 5 to 6 weeks or more and encyst on water vegetation, where they remain until eaten by the final host. The cercariae are not infective until about 12 hours after encysting. The cysts withstand short periods of drying. The young flukes normally reach the liver by burrowing through into the abdominal cavity and entering from the surface, but occasionally they get into the circulation and may be distributed to abnormal locations. According to Schumacher (1939), they bore into the liver parenchyma on the second to sixth day after infection but do not enter the bile passages until the seventh or eighth week. The worms live mainly on blood. Egg production begins in about 3 months and lasts for several years. One experimentally infected sheep passed eggs for 11 years. In time the bile passages inhabited by the flukes become very thickened, often with calcified walls, and normal liver function is seriously interfered with.

Olsen in 1943 confirmed the usefulness of hexachloroethane for treatment of cattle; he administered it in a drench with bentonite and water; at the rate of 10 grams of the drug per 100 lb. of weight he got 90 per cent cures with no ill effects. Kouri recommends emetin as a specific treatment in man.

In the Near East *Fasciola* has been considered the cause in man of a "parasitic laryngo-pharyngitis," or "halzoun," an acute irritation of the throat from temporary attachment of worms eaten with raw food; it is said to come from eating raw livers of sacrificial animals. Witenberg, however, thinks it is usually due to eating improperly cooked fish containing the large metacercariae of *Clinostomum*. Similar attacks are common in Japan. *Clinostomum* is normally parasitic in water birds. In this country the metacercariae in fish are called "yellow grubs"; their presence ruins vast numbers of fresh-water fish, especially perch, for food. Incidentally, another temporary fluke infection was found by the writer to be quite common in the state of Manipur in Assam, caused by eating raw swim bladders of catfish infected with

a large flat fluke, *Isoparorchis hypselobagri*, superficially resembling *Fasciolopsis*.

DICROCOELIIDAE

The Dicrocoeliidae are small flat flukes, with the testes in front of the ovary and the uterus looped far posteriorly. They have small eggs and stilet cercariae which develop in land snails. The adult worms live, with rare exceptions, in the bile ducts or pancreatic ducts of birds or mammals.

***Dicrocoelium dendriticum*.** This fluke (Fig. 73A) is a common liver parasite of sheep and other ruminants in many parts of the world, but particularly in Europe and Asia. Human cases are not infrequent, though often the presence of eggs in human feces is not due to infection but to ingestion of liver of infected animals. The effects are similar to those produced by *Fasciola*, but less severe.

This worm was first discovered in the United States in a cow from upper New York State in 1941; within 10 years it had become an important parasite of sheep and cattle in that area, and had established itself in woodchucks (marmots), deer, and cottontail rabbits as reservoir hosts. The life cycle was worked out by Krull and Mapes (1952, 1953) and found to involve a small land snail, *Cionella lubrica* (Fig. 73C) in which the long-tailed cercariae (*C. vitrina*) are continually being produced from germ masses in the daughter sporocysts. These collect in the respiratory chamber of the snail, hundreds of them being rolled together into a "slime ball," formed by secretion from the voluminous glands that fill the body of the cercariae, and hardened on the surface to form a sort of community cyst (Fig. 73D). These slime balls are dropped by the snail in its wanderings and are regarded by ants (*Formica fusca*) (Fig. 73E) as choice food items which they carry to their nests. Metacercariae develop in the ants and these, when eaten with vegetation, infect the definitive hosts, but the latter could not be infected by feeding them either snails or slime balls, contrary to results reported previously in Europe. Work by Vogel and Falcao in 1954 in Germany confirmed the necessary role of ants as second intermediate hosts. The adult flukes, which are 5 to 15 mm. long and only 1.5 to 2.5 mm. broad, live in the bile ducts, which Neuhaus (1938) said they reached via the portal blood system. Krull and Mapes found up to 50,000 flukes in the liver of old sheep.

***Eurytrema pancreaticum*.** This fluke (Fig. 73B) lives in the pancreatic ducts of pigs and in the biliary ducts of cattle, water buffaloes, and camels in China. Its thicker body and large oral sucker suffice to distinguish it from *Dicrocoelium*. A few human cases have

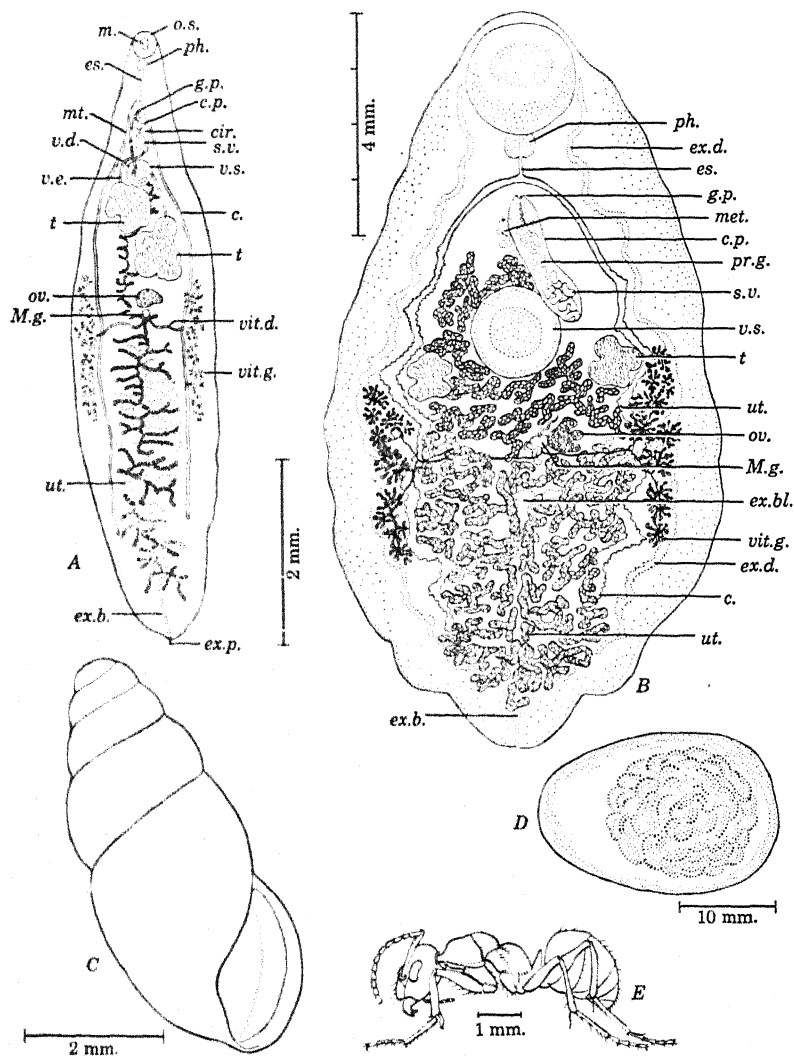


FIG. 73. A, *Dicrocoelium dendriticum*. B, *Eurytrema pancreaticum* (abbreviations as in Fig. 58). C, *Cionella lubrica*, first intermediate host of *D. dendriticum*. D, slime ball of same. E, *Formica fusca*, second intermediate host of same. Abbrev.: c., cecum; cir., cirrus; c.p., cirrus pouch; es., esophagus; ex.b., excretory bladder; ex.d., excretory duct; ex.p., excretory pore; g.p., genital pore; m., mouth; M.g., Mehlis' glands; met., metraterm; ph., pharynx; pr.g., prostate glands; o.s., oral sucker; ov., ovary; s.v., seminal vesicle; t., testis; ut., uterus; v.e., vas efferens; v.d., vas deferens; vit.d., vitelline duct; vit.g., vitelline glands; v.s., ventral sucker. (A, C, adapted from Mapes, D from Krull and Mapes, *Cornell Vet.*, 1952; B from Looss.)

been recorded from South China. This worm, also, develops in land snails. Tang (1950) showed that the mother sporocysts continually reproduce daughter sporocysts, but each of these produces only a few almost tailless cercariae, which all mature together and remain, as in a sac, in the thick-walled sporocysts, which are, eventually, shed by the snail. An intermediate host is probably needed. The known or suspected intermediate hosts of the few *Microcoeliids* thus far worked out include ants, beetles, isopods, and lizards, but lizards are more likely to be transport hosts.

OPISTHORCHIIDAE

The flat, elongate, semitransparent flukes of this family occur in fish-eating animals, particularly in Europe and Asia, but one species, *Metorchis conjunctus*, is very common in Canada, and *Amphimerus pseudofelineus* occurs in cats in the United States. The general arrangement of the organs can be seen from Figs. 74 and 75. The eggs of these flukes are very small and contain miracidia when laid, but the miracidia do not ordinarily hatch until eaten by a suitable snail. The cercariae have long fluted tails and no stylets; they encyst in freshwater fishes, and reach their final hosts when the fish are eaten.

***Clonorchis sinensis*.** This, the most important human parasite in the family, is widely distributed in the Far East from Korea and Japan through China to Indo-China and India. It is common in cats and dogs throughout its range, but human infection is limited to localities where raw fish is esteemed as food. Heavy human infections are common in local areas in Japan, in the vicinity of Canton and Swatow in China, and in the Red River delta in Indo-China. Stoll (1947) estimated about 19,000,000 human cases in all.

The adult flukes vary from 10 to 25 mm. in length and are 3 to 5 mm. wide, with an arrangement of organs as shown in Fig. 74D. The deeply branched testes distinguish this genus from the related *Opisthorchis*, in which the testes are round or lobed. The adults live both in the small biliary ducts of the liver and also in the larger bile ducts leading to the gall bladder, often in hundreds or even thousands.

LIFE CYCLE. The small yellow-brown eggs average 27 by 16 μ in size, the operculum fitting into a thickened rim of the shell like the lid on a sugar bowl (Fig. 74C). The miracidia hatch when eaten by small, conical, operculate snails of the subfamily Buliminae (formerly Bythiniinae) which belong to the family Hydrobiidae (see p. 272). The most important species are *Parafossarulus manchouricus* (= *P. striatulus*) (Fig. 74B) and *Bulinus fuchsianus*. One of the Thiariidae (see p. 272), *Hua ningpoensis*, is also an important snail host.

The miracidia develop into rounded sporocysts which produce rediae. The rediae give birth to cercariae (Fig. 74A) characterized by a long tail with a long dorsal and shorter ventral fins, finely spined cuticle, 7 pairs of penetration glands, 14 cystogenous glands, eye spots, and masses of brownish pigment. The cercariae encyst in the flesh of

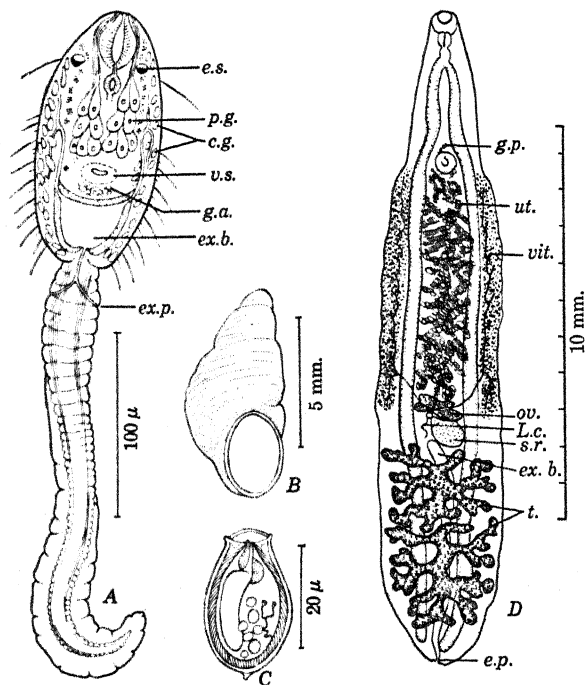


FIG. 74. *Clonorchis sinensis*: A, cercaria; B, snail host, *Parafoissarulus manchouricus*; C, egg containing miracidium (side view); D, adult; c.g., cystogenous glands; e.s., eye spot; ex.b., excretory bladder; ex.p., excretory pore; g.a., genital anlage; p.g., penetration glands; other abbreviations as in Fig. 58. (A, after Komiya and Tajimi, *J. Shanghai Sci. Inst.*, February, 1940. B and C adapted from Faust and Khaw, *Am. J. Hyg. Monogr. Ser.*, 8, 1927.)

fresh-water fishes and develop into metacercariae which lose the eye spots and have the sac-like excretory bladder filled with coarse, refractile granules. The cysts are oval with thin walls, and average 138 by 115 μ .

Numerous species of fresh-water fish, most of them of the minnow and carp family (Cyprinidae), serve as second intermediate hosts. According to Hsü the metacercariae normally encyst in the flesh and only exceptionally under the scales or in the gills. When infected fish

are eaten raw the metacercariae are liberated and enter the bile duct within a few hours after being eaten.

Migration to the liver via the bile duct by the Opisthorchiidae is in contrast to the route taken by *Dicrocoelium* via the portal veins or by *Fasciola* through the intestinal wall and abdominal cavity. It takes about 3 weeks for the flukes to reach maturity and to begin shedding eggs.

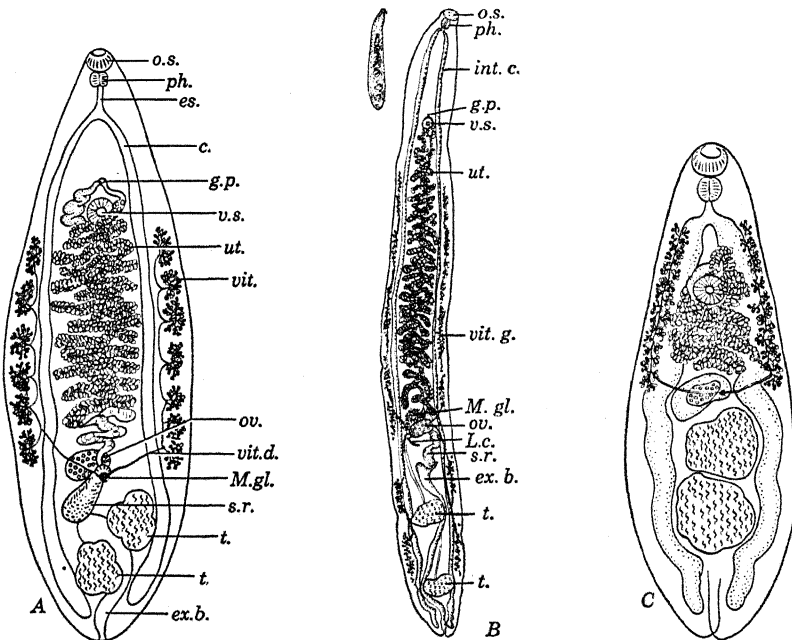


FIG. 75. A, *Opisthorchis felineus*, $\times 5$; B, *Amphimerus pseudofelineus*, $\times 5$; C, *Metorchis conjunctus*, $\times 20$; abbreviations as in Fig. 58 on page 261. (B, adapted from Barker.)

EPIDEMIOLOGY. Observations by Faust and Khaw in infected localities show how *Clonorchis* infections thrive. In the mulberry-growing areas near Canton, latrines are placed over fish ponds, feces falling directly into the water or onto night-soil rafts. Suitable snails occur in the ponds and feed on the fecal material, the fish are later attacked by the cercariae, and the people become infected when they eat the raw fish sliced with radishes or turnips and highly seasoned. The fish are often not eaten entirely raw, but are laid on top of a dish of steaming rice where they are heated sufficiently to remove the raw taste, but not enough to kill cysts in the interior of the flesh. Others merely dip

the fish into hot "congee" with similar results. The cysts are unaffected by vinegar or sauces.

Clonorchis infections have been found in Orientals in all parts of the world, but two factors are necessary for it to become endemically established: (1) the presence of a suitable snail to serve as an intermediate host, and (2) the habit of eating raw fish. No suitable snail hosts are known to occur in the United States, and, even if they did, the failure of Americans to appreciate the gastronomic virtues of raw fish would prevent spread of *Clonorchis* as a human parasite beyond a few colonies of Orientals. A potential intermediate host in the United States is *Bulinus tentaculatus* in the Great Lakes region, since a member of this genus, *B. fuchsianus*, serves as a host in the Orient.

THE DISEASE AND ITS TREATMENT AND PREVENTION. The flukes injure the epithelium of the biliary ducts, and if numerous they may seriously clog them. The walls of the ducts become thickened, and neighboring portions of the liver tissue may be involved, in severe cases leading to a general cirrhosis. Light infections may show no symptoms at all; more severe infections are accompanied by diarrhea, often with blood, edema, enlarged liver, and abdominal discomfort.

Treatment is uncertain. Some workers have obtained good results with injections of antimony compounds, but complete cures are not usually obtained. Faust and Khaw found that complete cures could be effected in early cases by gentian violet and related dyes given in the form of coated pills, and that even in cases of long standing a proportion of the worms could be reached by a sufficient concentration of the dye to kill them. Recently a fairly high degree of success has been obtained in treatment of *Opisthorchis viverrini* with Chlorquine diphosphate, in a total of about 7 grams over a period of about 3 weeks, and it seems probable that such treatment would be equally effective for other opisthorchiids.

Prevention would be possible by storing night soil undiluted or adding 10 per cent of ammonium sulfate to kill the eggs before snails got access to them. Susceptibility of the fish to copper sulfate prohibits its use for snail destruction. The best preventive measure is to prohibit the sale of raw fish in public eating places and to educate people to the dangers of eating raw fish. However, it is never easy to suppress well-established tastes in food, and, besides, the cost of fuel for cooking is in some places a real economic factor.

***Opisthorchis* spp.** The genus *Opisthorchis*, differing from *Clonorchis* in having round or lobed testes (Fig. 75A), contains several species of flukes that are parasitic in cats and dogs and related animals, and sometimes in man. One very widespread and common species is

O. felineus, found from central and eastern Europe to Japan; in some parts of its range it is a common human parasite. It is about 7 to 12 mm. long and 2 to 3 mm. broad, with habits similar to *Clonorchis*. Vogel (1934) found the snail host in East Prussia to be *Bulinus tentaculatus* (= *Bythinia leachi*) (Fig. 76D), and the principal fish host the tench. The eggs (Fig. 76C) are more slender than those of *Clonorchis*, averaging about 30 by 14 μ . According to Vogel, the miracidia hatch in the gut of the snail and grow into slender sporocysts, which produce numerous rediae over a period of several months; these in turn produce the cercariae. The latter (Fig. 76A,B) are born in an undeveloped state and finish their development in the tissues of the snails, eventually leaving the snail after several months.

After penetrating certain fish hosts, for which they show distinct preferences, the cercariae burrow into the tissues and secrete a cyst wall within 24 hours, but it appears to require about 6 weeks of ripening before the metacercariae are infective. During this time they grow to three or four times their original size. Ripe cysts measure about 300 by 200 μ , with a cyst wall about 20 μ thick. As with other members of the family, the liberated metacercariae reach the liver via the bile duct.

Other species, *O. viverrini* in southeastern Asia, *O. noverca* in India, and *O. guayaquilensis* in Ecuador, have similar habits and have also been recorded from man. *O. viverrini* is very common in parts of Thailand, where it is estimated that 1,500,000 people are infected.

Other Opisthorchiidae. The genus *Amphimerus*, distinguished from *Opisthorchis* by having a postovarian division of the yolk glands, contains a species, *A. pseudofelineus* (Fig. 75B), found in cats and coyotes in central United States. The genus *Metorchis* contains flukes that are shorter and broader than *Opisthorchis*, with a rosette-shaped uterus (Fig. 75C). Cameron (1939, 1944) reported the common occurrence of *M. conjunctus* over a wide area in Canada east of the Rockies. It is a small fluke, 1 to 6.6 mm. long, found naturally in dogs, foxes, cats, mink, and raccoons, and occasionally in man, and is injurious to fur-bearing animals. The snail host is *Amnicola limosa porata*,

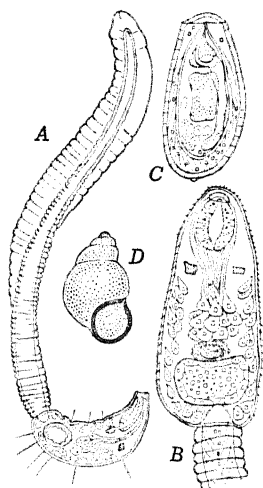


FIG. 76. *Opisthorchis felineus*: A, cercaria hanging in characteristic "pipe stem" manner, $\times 200$; B, body of cercaria, $\times 320$; C, egg containing miracidium, $\times 1000$; D, snail host, *Bulinus tentaculatus* (= *Bythinia leachi*), $\times 3\frac{1}{2}$. (Adapted from Vogel, *Zoologica*, 33, 1934.)

and the metacercariae encyst in the flesh of the common sucker, *Catostomus commersonii*, sometimes in great numbers.

The pathogenic effects, treatment, and epidemiology of these infections do not differ in any way, so far as known, from those of *Clonorchis* (see pp. 309–310).

Intestinal Flukes

The great majority of flukes inhabit the intestine of their hosts, yet there are no flukes that can be considered *primarily* parasites of the human intestine. A few species are very commonly found in man in some localities, though primarily parasitic in other animals, but the majority that have been reported from man are rather rare or accidental infections. On account of the omnivorous and variable food habits of the human being, he is subject to a wide range of such accidental parasites, including species properly belonging to both carnivorous and herbivorous hosts; probably no animal except the pig can compete with man in this respect.

We shall consider the following groups or species of intestinal flukes: (1) amphistomes (families Gastrodiscidae and Paramphistomatidae), normally parasitic in herbivores; (2) *Fasciolopsis* (family Fasciolidae), normally in pigs; (3) Heterophyidae, normally in fish-eating birds and mammals; (4) echinostomes (family Echinostomatidae), commonly parasitic in aquatic birds and mammals; and (5) a few other families which contain important intestinal parasites of lower animals, and sometimes rarely of man—the Strigeidae, Clinostomatidae, Troglorematidae, and Plagiorchiidae.

AMPHISTOMES

Long considered a distinct suborder, Amphistomata, this group of flukes is characterized by having the ventral sucker near the posterior end. A few are found in cold-blooded vertebrates and birds, but most of them live in the rumen or intestine of herbivorous mammals, literally carpeting considerable areas. Most of those in mammals belong to the families Gastrodiscidae, which have a large ventral disc (Fig. 77A), and Paramphistomatidae (Fig. 77C and D), which are superficially maggot-like in appearance.

***Gastrodiscoides hominis*.** This member of the Gastrodiscidae is the only amphistome found at all frequently in man; it is a common parasite of pigs in India. Buckley (1939) found it in over 40 per cent of 221 people examined in three villages in Assam, where it is probably widely disseminated. By means of soap-water enemas he obtained nearly 1000 worms from an 8-year-old boy. Although it

is present in 50 per cent of pigs in some places in Bengal and Assam, pigs were rare in the locality visited by Buckley and could hardly have served as a reservoir. Human infections have also been reported from Annam.

The worm inhabits the cecum and large intestine of its host, where it causes some inflammation and diarrhea. The adults (Fig. 77*A* and *B*), 5 to 7 mm. in length when preserved, have an orange-red appearance

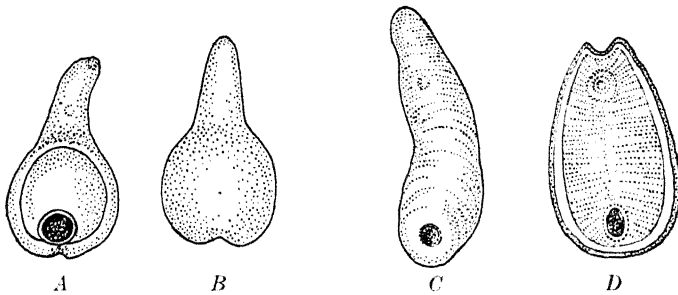


FIG. 77. Amphistome flukes: *A* and *B*, *Gastrodiscoides hominis*, ventral and dorsal views; *C*, *Paramphistomum cervi*, ventral view; *D*, *Watsonius watsoni*, ventral view, about $\times 4$. (*D* after Stiles and Goldberger, *Hyg. Lab. Bull.*, 60, 1910.)

when living, caused by a fine network of bright red capillary-like lymphatics in the cuticle, against a flesh-colored background. The body is divided into two parts—a very active, slender, conical or finger-like anterior portion which has the genital pore on its ventral side, and an almost hemispherical posterior portion, scooped out ventrally in a disc-like manner, with a sucker near its posterior border and a notch at the posterior end. Several closely related species in the genus *Gastrodiscus* occur in the intestines of horses and pigs in Africa.

The eggs (Fig. 57) are very large, as are those of other amphistomes, and rather rhomboidal in shape, tapering rapidly towards each end. The miracidia develop after the eggs have escaped from their host, but nothing is known of the life cycle beyond this point. By analogy with other amphistomes, there is little doubt that the cercariae encyst on water vegetation, and that the life cycle is essentially similar to that of the Fasciolidae. *Gastrodiscoides* is not easily removed by anthelmintics but sometimes responds to soap-water enemas.

Watsonius watsoni. This fluke (Fig. 78*A*), the only other amphistome thus far found in man, has been recorded but once, from the small intestine of an emaciated Negro who died from severe dysentery in Nigeria; its normal hosts appear to be monkeys, in which the parasite has been found in Africa, Malaya, and Japan. The worm when living

is reddish yellow; it is a thick, pear-shaped animal, about 8 to 10 mm. long, slightly concave ventrally, with a translucent gelatinous appearance. It belongs to the family Paramphistomatidae, which contains many species parasitic in the rumen of ruminants. *Paramphistomum cervi* is widespread in the Old World, but *Cotylophoron cotylophoron*

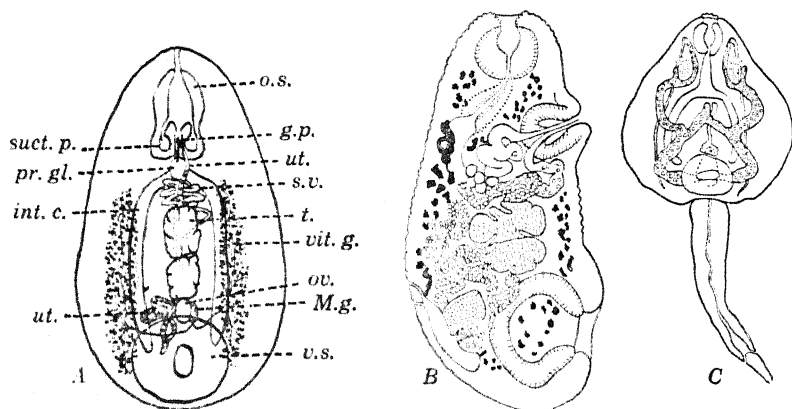


FIG. 78. Amphistomes. A, *Watsonius watsoni*, $\times 6$, showing internal anatomy; *suct. p.*, suctorial pouch; other abbreviations as in Fig. 58. B, *Cotylophoron cotylophoron*, side view; C, same, cercaria (excretory ducts with granules, eye spots lateral to esophagus). A, after Stiles and Goldberger, *Hyg. Lab. Bull.*, 60, 1910. B, after Fischöder from Travassos, 1934. C, from Bennett, *Ill. Biol. Mon.*, 14, 1936.)

(Fig. 78B,C) is the common species in southern United States. Its life cycle was found by Bennett (1936) to be very similar to that of *Fasciola*. Light amphistome infections are practically harmless, but in heavy infections cattle develop diarrhea, lose weight, and fall off in milk production.

FASCIOLOPSIS BUSKI

Another parasite which man shares with pigs is *Fasciolopsis buski*, a member of the family Fasciolidae (see p. 302). This is a large flat fluke (Fig. 79K), creamy pink in color, which reaches a length of 2 to 7.5 cm. When preserved it contracts and thickens, but fresh, relaxed specimens are rather thin and flabby. In general arrangement of organs it resembles *Fasciola*, but it has no thickened cone at the anterior end, and has unbranched intestinal ceca. It is widely distributed in pigs in southeast Asia from central China to Bengal and in many of the East Indian Islands. Stoll (1947) estimated a total of 10 million human infections, most of them in China, though there are a few endemic localities in Assam and Bengal. In some villages near Shaohsing,

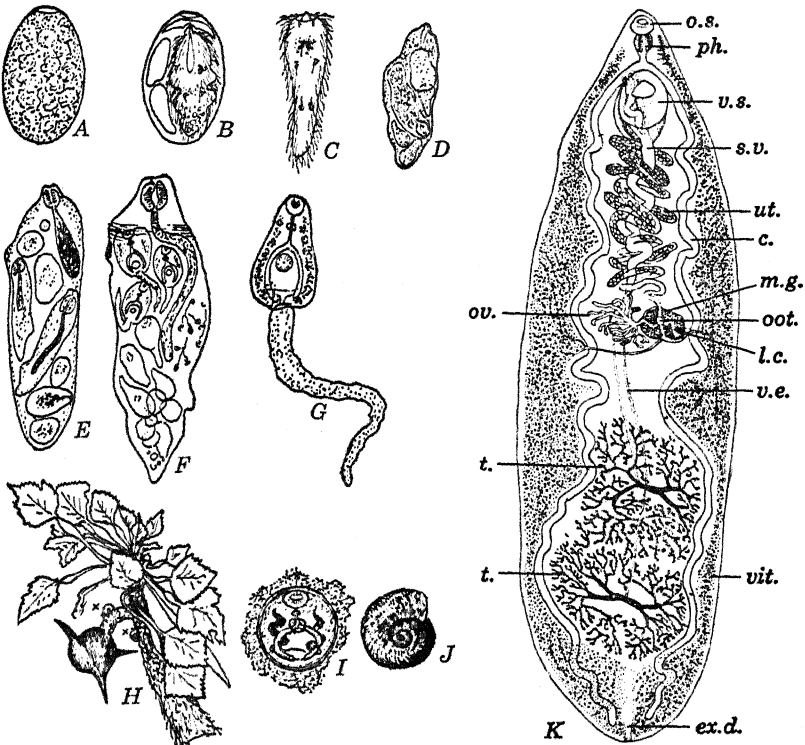


FIG. 79. Stages in life cycle of *Fasciolopsis buski*. A, egg as passed in feces, showing yolk balls; B, egg containing developed miracidium, with "mucoid plug" at anterior end and oil globules at one side; C, miracidium, showing eye spots; D, sporocyst containing developing mother rediae; E, mother redia containing developing daughter rediae; F, daughter redia containing developing cercariae; G, cercaria; H, Chinese caltrop or water ling (*Trapa natans*) with snails at points marked "X"; I, encysted metacercaria; J, *Segmentina hemisphaerula*, intermediate host; K, adult fluke. A-D, $\times 140$; E, $\times 50$; F, $\times 40$; G and I, $\times 70$; H, $\times 1\frac{1}{2}$; J, $\times 11\frac{1}{2}$; K, $\times 2$. (A-J sketched from figures by Barlow, *Am. J. Hyg. Monogr. Ser.*, 4, 1925. K from Brown, *Synopsis of Medical Parasitology*, 1953.) (Abbreviations as in Fig. 58, p. 261.)

China, according to Barlow, 100 per cent of the people examined were found to be infected. The eggs (Fig. 79A) are large and very variable in size but average about 138 by 83 μ . The miracidia require several weeks to develop after they are passed by the host. The intermediate hosts are members of the family Planorbidae, principally small, flatly coiled, aquatic snails, *Segmentina hemisphaerula* (Fig. 79J) and *Hippeutis contori*.

In the snails the miracidia change into sporocysts, which are peculiar in possessing a sac-like gut like a redia, but no pharynx. Two genera-

tions of rediae are produced, the second generation of which produce large heavy-tailed cercariae (Fig. 79G), measuring, with the tail, nearly 0.7 mm. in length. These begin leaving the snail after about a month. The free-swimming life is brief, occupying only time enough for the cercaria to get to the plant on which the snail is feeding. In 1 to 3 hours the cercaria has lost its tail and has encysted. The cysts are pearly white and about 200 μ in diameter. The whole development from infection of snails to encystment takes 5 to 7 weeks.

✓ **Mode of Human Infection.** In China, human infection has been traced mainly to the eating of the nuts of a water plant known as the red caltrop or red ling (*Trapa natans*) (Fig. 79H), on the pods of which the cercariae encyst. These plants are extensively cultivated in ponds in the endemic areas and are fertilized by fresh night soil thrown into the water. The little snails abound in these warm stagnant pools; the plants are fairly alive with snails creeping over their stems and leaves. The nuts are eaten both fresh and dried. When fresh they are kept moist and are peeled with the teeth, during which process the cysts gain access to the mouth and are swallowed. Barlow examined nuts from typical ponds, and found a few to over 200 cysts on each nut. The writer (1928) traced some cases of infection in eastern Bengal to the eating of a water nut, *T. bicornis*, closely related to the Chinese nut; there is another focus of infection in India in northern Bihar. Another plant carrying infection is the so-called water chestnut, *Eliocharis tuberosa*, which has tubers like gladiolus bulbs.

✓ **Pathology.** *Fasciolopsis buski* usually lives in the small intestine, where it causes local inflammation, with bleeding and formation of ulcers. Symptoms develop about 3 months after infection. There is first a period of latency during which there is some asthenia and mild anemia. This is followed by diarrhea, a marked anemia, and usually some abdominal pain. The combination of chronic diarrhea and anemia, together with a distended abdomen, edema of the legs and face, and stunted development, is characteristic of a long-standing infection. In heavy infections the continued diarrhea and edema lead to severe prostration and sometimes death.

According to Barlow, *F. buski* is easily got rid of by a number of different drugs, among which he includes oil of chenopodium, beta-naphthol, thymol, and carbon tetrachloride, but some of these drugs would be too toxic for many persons weakened by this infection. Hexylresorcinol crystoids given as for *Ascaris* infections (see p. 446) give excellent results. Probably tetrachloroethylene, given as for hookworm infections, would also be effective.

Prevention consists in educating the people of endemic areas to the

danger of eating fresh-water ling, water chestnuts, or other water vegetables unless they are cooked or at least dipped in boiling water. Sterilization of night soil would also be effective, but that presents a vastly more difficult problem.

HETEROPHYIDAE

The flukes of this family are extremely small, sometimes only 0.5 mm. in length, and egg-shaped; they are normally parasitic in fish-eating animals. They have the cuticle covered with minute scale-like spines. The genital pore opens into a retractile sucker-like structure which

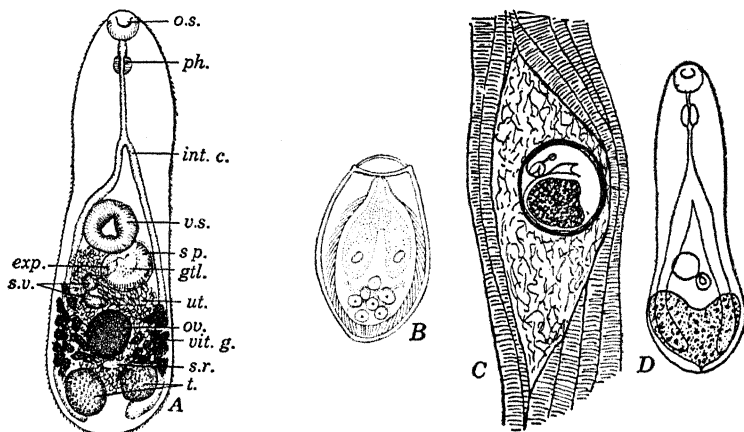


FIG. 80. *Heterophyes heterophyes*. A, adult fluke, $\times 40$; gtl., gonotyl; sp., spines of gonotyl; other abbreviations as in Fig. 58 on p. 261. B, egg, $\times 900$. C, metacercaria encysted in muscles of mullet, $\times 60$. D, metacercaria freed from cyst, $\times 50$. (B, after Nishigori, *Taiwan Igak. Zasshi*, 1927. C and D, after Witenberg, *Ann. Trop. Med. Parasitol.*, 23, 1929.)

is either incorporated in the ventral sucker or lies to one side of it; Witenberg called this structure a "gonotyl." The arrangement of organs can be seen from Figs. 80 and 81. The life cycle is practically the same as that of the Opisthorchiidae, and a closely related group of snails serve as intermediate hosts.

The eggs (Fig. 80B) are very small, being in most species about 20 to 35 μ in length by 10 to 20 μ in diameter. They resemble the eggs of *Clonorchis*, and contain developed miracidia. Hatching occurs when the eggs are eaten by the proper species of snails. As far as known these are species of Thiariidae (see p. 272) in the Far East, but in the Middle East *Pirenella* (family Potamididae) is the host of *Heterophyes heterophyes* and other heterophyids. In the snails two generations of rediae are produced.

The cercariae have eye spots and large tails with fluted lateral fins; they are strikingly like those of the Opisthorchiidae but have a special arrangement of spines around the mouth. After leaving the snail host the cercariae usually encyst in fishes, mullets being especially favored, but one species has been found to encyst in frogs as well. Development in the final host is very rapid, maturity being reached in 7 to 10 days.

Host-Parasite Relations. Numerous species of Heterophyidae have been described. They all seem remarkably versatile with respect to the hosts in which they can mature, but their behavior in abnormal hosts suggests that they feel uncomfortably out of place—in the right pew but in the wrong church, as it were. Faust and Nishigori (1926) found that certain heterophyids of night herons, when experimentally fed to mammals, gradually shifted their position farther and farther back in the gut until finally expelled. Another and more important reaction was observed by Africa, Garcia, and de Leon in 1935. They noted the tendency of various species in the Philippines, when infecting dogs and man, to become buried deep in the mucous membranes. The eggs, instead of escaping normally in the feces, are taken up by the lymphatics or blood vessels and distributed over the body. Often the worms die imprisoned in the tissues. In an American species, *Cryptocotyle lingua*, studied by Stunkard (1941), no actual invasion of the tissues was noted, although there was much tissue damage, especially in abnormal hosts.

Injury to Heart and Other Viscera. Africa et al. (1940) showed that eggs of "foreign" species of Heterophyidae distributed over the body may cause serious injury. The most frequent damage is in the heart, where the eggs are deposited in large numbers. A dropsical condition and acute dilatation of the heart may result, producing symptoms similar to cardiac beri-beri and often fatal. The eggs were also found in the brain and spinal cord, where they are associated with grave nervous symptoms.

The species of Heterophyidae causing these conditions belong to a number of different genera, including *Heterophyes*, *Haplorchis* (Fig. 81, left), and *Diorchitrema*. *Haplorchis yokogawai*, measuring about 0.7 by 0.28 mm., is the species most frequently causing trouble in man in the Philippines. This species is reported as a common parasite of cats and dogs and occasionally of man. It is possible that the smaller species of Heterophyidae are the most likely to invade the mucosa.

NORMAL INTESTINAL HETEROPHYIDS OF MAN. Two species, *Metagonimus yokogawai* and *Heterophyes heterophyes*, may be regarded as normal parasites of man and other mammals, since they appear to lead

an orthodox life in the lumen of the intestine and are very common human parasites in certain localities.

M. yokogawai (Fig. 81, right) is a common parasite of dogs and cats in Japan, Korea, China, Palestine, and the Balkans. Human infection is frequent in Japan and in eastern Siberia. Like other members of the family, this tiny fluke is not very particular about its final host, for it infects not only carnivores, pigs, and man, but also pelicans and, experimentally, mice.

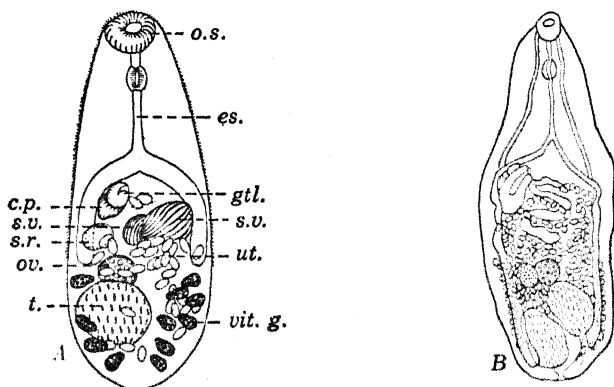


FIG. 81. A, a species of *Haplorchis*, about $\times 100$; gtl., gonotyl; other abbreviations as in Fig. 58, p. 261. (After Africa and Garcia, *Philip. J. Sci.*, 53, 1935.) B, *Metagonimus yokogawai*. (Adapted from Mönnig, *Veterinary Helminthology and Entomology*, Williams and Wilkins, 1949.)

The adult worms live in the duodenum, sometimes by thousands. They are only 1 to 2.5 mm. in length and about 0.5 mm. broad. A characteristic feature is the displacement of the ventral sucker to the right side of the body, with the genital opening in a pit at the anterior border of it. The eggs are about 28 to 30 μ by 16 to 17 μ . The snail intermediate hosts are species of *Thiaridae* (see p. 272). The cercariae attack fresh-water fishes, particularly a species of trout, *Plecoglossus altivelis*, and infection of the final host occurs when the uncooked fish are eaten. The cysts are discoidal and found principally in pockets under the scales.

H. heterophyes (Fig. 80A) is also a very small fluke; relaxed specimens in dogs measure up to 2.7 mm. by 0.9 mm., but in cats they are only about 1.3 by 0.3 mm. They have the ventral sucker on the median line, with a separate spiny genital sucker to the right of it. These flukes are common in cats, dogs, and allied animals in Egypt, Palestine, Yemen, India, and the Far East. Human infections are common both in the Far East and in Egypt and Palestine.

Khalil in 1933 found a common marine and brackish water operculated snail, *Pirenella conica*, to be the snail host in Egypt. The cercariae encyst under the scales and in the flesh of mullets, especially *Mugil cephalus*, and rarely in other fish; in one mullet from the fish market in Jerusalem, Witenberg found over 1000 cysts per gram of flesh. The round cysts (Fig. 80C) lie in spindle-shaped masses of fat globules and measure 0.13 to 0.26 mm. in diameter. The metacercariae, lying folded inside, have the anterior part of the body flattened.

Pathology. In infections with the normal human species the symptoms are usually negligible, though in heavy infections there may be mild digestive disturbances and diarrhea.

Like other intestinal flukes, these species are susceptible to the group of anthelmintics used for nematodes, but their small size and ability to hide away between the villi make treatment unsatisfactory unless the intestine is thoroughly cleaned of contents and mucus beforehand. Prevention consists in eschewing raw infected fish.

NANOPHYETUS SALMINCOLA

These small flukes (Fig. 82), 1 mm. or less in length, belong to the same family as *Paragonimus*, Troglotreumatidae. They are common parasites of fish-eating mammals in northwestern United States, the

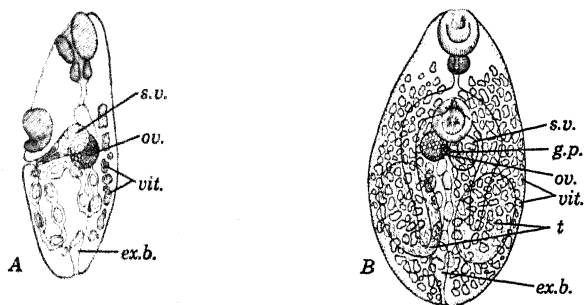


FIG. 82. *Nanophyetus salmincola*. A, lateral view; B, ventral view; abbreviations as in Fig. 58. (Adapted from Witenberg, *J. Parasitol.*, 18, 1932.)

metacercariae encysting in salmon. The snail host in Oregon, according to Donham, Simms, and Shaw (1932), is *Goniobasis silicula*, a common species in running water. The cercariae resemble those of *Paragonimus*. Dogs and foxes are the best definitive hosts. Human infection has been reported from eastern Siberia.

This parasite is of particular interest because it is associated with a highly fatal disease of dogs called "salmon poisoning." Simms et al.

(1932) showed that the disease was caused by an infectious organism transmitted by the metacercariae of *Nanophyetus salmincola* when eaten with the flesh of salmon. It was at first thought to be a virus but was later shown to be a rickettsia-like organism, *Neorickettsia helmintheca* (see p. 230). After an incubation period of a week or more there are loss of appetite, fever, and sensory depression, followed by edema, violent vomiting, and dysentery. If diagnosed within 3 hours of onset, 2 to 6 mg. of apomorphine by mouth is protective. Animals that recover become immune. As yet this disease has not been observed in man.

ECHINOSTOMES 1936

The family Echinostomatidae includes numerous species of flukes parasitic in many kinds of vertebrates, particularly aquatic birds. Most species are characterized by a spiny body and a collar of spines near the anterior end. Most of them, like the Heterophyidae, are remarkably promiscuous as to their final hosts, and many are not very particular about their snail hosts, either.

The eggs are large, usually over $100\ \mu$ long, and contain partly developed embryos when laid; the miracidia have a median eye spot and develop in water. In their snail hosts, usually planorbids, Johnston in 1920 believed the miracidia to develop directly into rediae, omitting the sporocyst stage, but actually, at least in some species, a single mother redia develops in the miracidium and gives rise to daughter rediae. The cercariae (Figs. 62D, 83A²) have well-developed tails and usually bear a collar of spines similar to that of the adults. Some species encyst directly in their snail hosts, sometimes in the body of their parent redia; others leave the snail that spawned them and encyst in other snails or in bivalves, insects, frogs, fishes, or on vegetation. The metacercarial cysts are oval or round, and only about 70 to $150\ \mu$ in diameter (Fig. 83A³); the contained metacercariae are folded and show two branches of the excretory bladder filled with coarse granules; the collar of spines can be seen on careful examination.

A number of species of echinostomes have been recorded from man, but most are rare and purely accidental parasites.

Echinostoma ilocanum is common in the Ilocanos of the Philippines and was found by Sandground in Java. It is 2.5 to 10 mm. long and 0.5 to 1.5 broad, with 51 collar spines. It is primarily a parasite of field rats, but Chen in 1934 found it common in dogs in Canton. The cercariae of this species after leaving the small planorbid snail, *Gyraulus prashadi*, commonly encyst in a large operculated snail, *Pila luzonica*, which the Ilocanos enjoy eating raw.

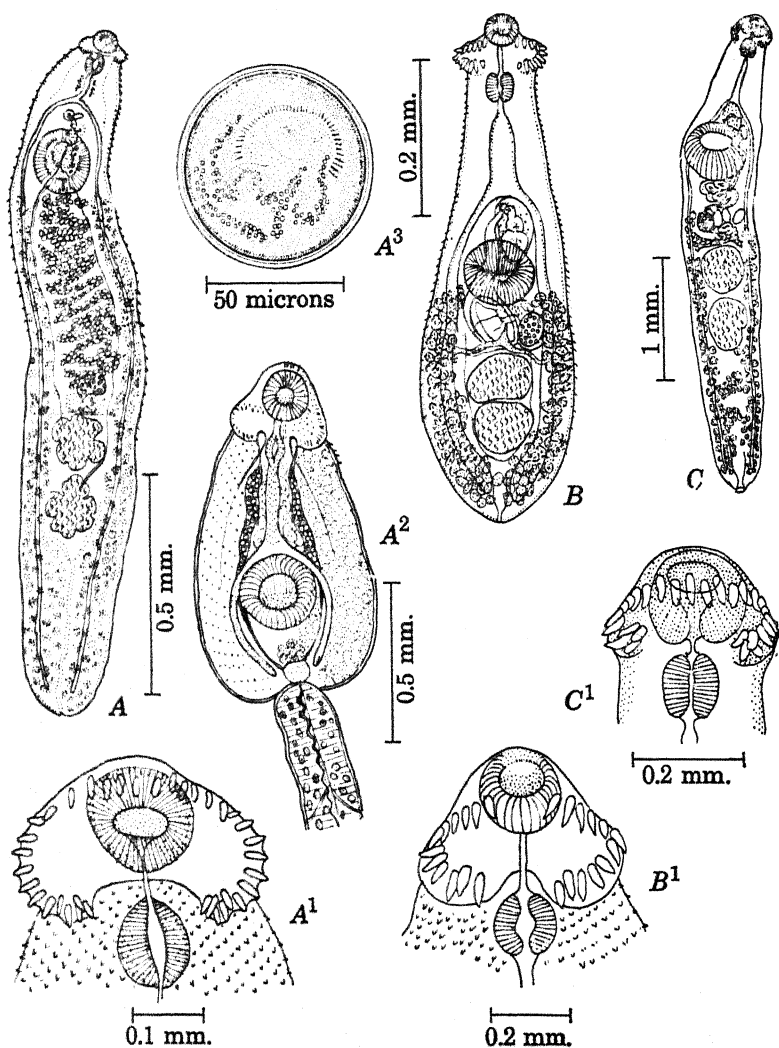


FIG. 83. Echinostomes. A, *Echinostoma lindoense*; A¹, head of same; A², cercaria of same. (After Sandground and Bonne, *Am. J. Trop. Med.*, 20, 1940.) A³, encysted metacercaria of *E. ilocanum*. (After Tubangui and Pasco, *Philip. J. Sci.*, 51, 1933.) B, *Echinochasmus japonicus*; B¹, head of same. (After Yamaguti.) C, *Euparyphium melis*; C¹, head of same. (After Beaver, *J. Parasitol.*, 27, 1941.)

E. malayanum, a broader fluke (5 to 10 mm. by 2 to 3.5 mm.) with 43 collar spines, another Far Eastern species, is common in certain tribes who live on the Sino-Tibetan frontier and has also been reported from Malaya and Sumatra.

In central Celebes, Sandground and Bonne (1940) found a high incidence of infection with another echinostome, *E. lindoense* (Fig. 83A, A¹) which is larger (13 to 16 mm. by 2 to 2.5 mm.) with only 37 collar spines. This was at first thought to be a primary human parasite, but Bonne and Lie later reported it as a parasite of ducks and other fowl. Infection results from eating lake mussels in which the metacercariae are encysted.

E. revolutum, a world-wide parasite of ducks and geese, is a sporadic human parasite. It is a small species with 37 collar spines. In Formosa it is said to affect 3 to 6 per cent of the people, a penalty for eating raw fresh-water mussels. Five cases have been reported from Mexico and a few from Java.

Other Echinostomatidae which occasionally crop up in man are: *Euparyphium melis* (= *E. jassyense*) (Fig. 83C, C¹), with 27 spines and a short uterus with few eggs, usually found in carnivores; *Echinoparyphium recurvatum*, with 45 spines, usually in birds; *Echinostoma macrorchis* and *cinetorchis* of rats in Japan; *Paryphostomum sufraginifex* of pigs in India; two species of *Echinochasmus* (a genus containing species with a collar of less than 20 spines, broken dorsally) — *E. perfoliatus* of dogs and cats in Europe and India and *E. japonicus* (Fig. 83B, B¹) of the same animals in Japan; and *Himasthla muhlensi*, probably of a marine bird of the eastern United States coast, which is very elongate and has a cirrus pouch extending far behind the ventral sucker.

STRIGEIDS

The strigeids, belonging to the families Strigeidae, Diplostomatidae, and several related families, are characterized by having a special "hold-fast organ" (Fig. 84, h.f.) on the ventral side, provided with histolytic glands; the body is usually divided more or less distinctly into a mobile fore body, and a hind body containing the reproductive organs (Fig. 84). They are common parasites of aquatic birds or fish- or frog-eating mammals. In life cycle they closely parallel the schistosomes, having miracidia with two pairs of flame cells, daughter sporocysts instead of rediae, and forked-tailed cercariae. The cercariae, however, are usually distinguishable from those of schistosomes by having a pharynx and by burrowing into a second intermediate host, usually fish, tadpoles, frogs, or water snakes. The metacercariae are often very

harmful to fish, since some species encyst in the lens or chambers of the eye, in the spinal cord, or around the heart; some encyst in the skin or muscles, causing "black spot." A typical life cycle has been graphically illustrated by the Hunters (1935).

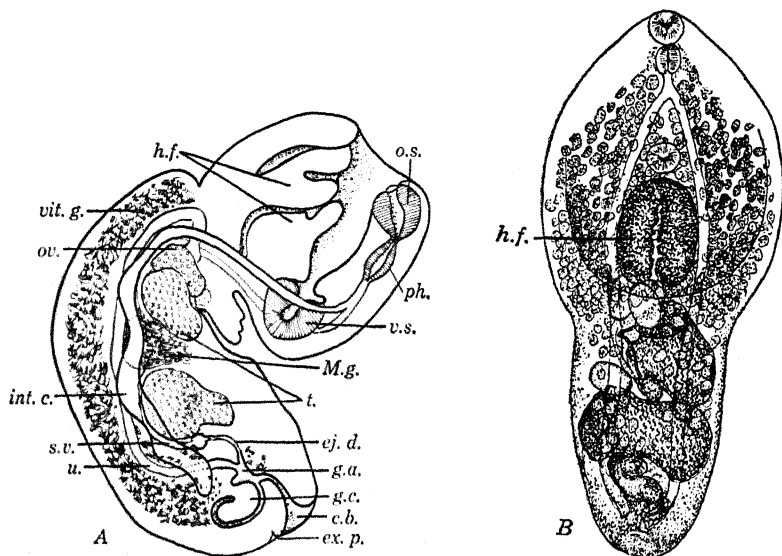


FIG. 84. Two types of strigeids: *A*, *Cotylurus flabelliformis* of ducks, example of Strigeidae; *B*, *Fibricola texensis* of raccoons, example of Diplostomatidae. Note pouch-like character of forebody in *A*, and holdfast organ (*h.f.*) in form of anterior and posterior transverse lips, whereas in *B* the forebody is spatulate and the holdfast organ oval; *c.b.*, copulatory bursa; *ej.d.*, ejaculatory duct; *g.a.*, genital atrium; *g.c.*, genital cone; *h.f.*, holdfast organ. Other abbreviations same as in Fig. 58, p. 261. (*A*, adapted from Van Haitsma, *Papers Mich. Acad. Sci., Arts, Letters*, 13, 1930. *B*, from Chandler, *Trans. Am. Micr. Soc.*, 61, 1942.)

These parasites when numerous may be very injurious in the intestines of their final hosts. Fortunately man is rarely parasitized by them, but Nasr (1941) called attention to human infection with an Egyptian species, *Prohemistomum vivax*, properly a parasite of kites, but also extremely common in dogs and cats which eat, or are fed, raw Nile fishes or tadpoles. One man with 2000 specimens complained of dysenteric symptoms.

PLAGIORCHIIDAE

This and a number of closely related families include numerous parasites of various insect-eating vertebrates, especially cold-blooded vertebrates. All have stylet cercariae which encyst in arthropods or

vertebrates. Since even a single species, *Plagiorchis muris*, will develop in such a variety of hosts as pigeons, shorebirds, muskrats, mice, and men, it is not surprising that several species of this genus have been reported from man in various parts of the world.

The only important species in domestic animals are members of the genus *Prosthogonimus*, which inhabit the oviduct and bursa fabricii of birds. Several species, including *P. macrorchis* (Fig. 85) in north

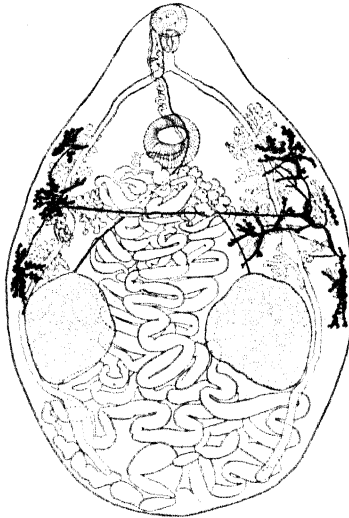


FIG. 85. *Prosthogonimus macrorchis*, oviduct fluke of poultry. $\times 18$. (After Macy, Univ. Minn. Agric. Exp. Sta. Bull., 98, 1934.)

central United States, are important parasites of poultry, causing a marked falling off in egg production and sometimes fatal disease. The cercariae of these flukes, after developing in snails (*Amnicola*), encyst in dragonfly nymphs or other aquatic insect larvae. Birds become infected by eating either nymphs or adults of dragonflies.

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The Cestoidea or Tapeworms

General Structure. Except in a few primitive species a mature tapeworm is not an individual, but a whole family, consisting sometimes of many hundreds of individuals one behind the other like links of a chain (Fig. 86). The most striking feature is the complete lack of a digestive tract in all stages of development. Larval forms obviously absorb food from the host's tissues through their exposed surfaces, but it has usually been assumed that adult tapeworms in the intestine subsist by absorbing digested but unassimilated foods from the fluid intestinal contents in which they live. The writer (Chandler, 1943), however, showed that, though this may be true for carbohydrates, most other food essentials are apparently absorbed from the host's mucous membranes with which the worms lie in contact. When many worms are present, crowding limits their contact and interferes with their nutrition, stunting their growth. Tapeworms are dependent on some constituent of yeast in the host's diet (Addis and Chandler, 1944; Beck, 1951) and also on sex hormones in the host (Addis, 1946; Beck, 1951; Aldrich, 1954).

In the subclass Cestodaria no chain of segments is formed, and there is only one set of reproductive organs; this is true also of one order, Caryophyllidea, allied to Pseudophyllidea, but all other tapeworms consist of chains of segments with a "head" or scolex for attachment at one end. Just behind the scolex is a narrow region or "neck" which continually grows and, as it does so, forms partitions, thus constantly budding off new segments. The segments, however, remain connected internally by the musculature and also by nerve trunks and excretory tubes. As the newly formed segments push back the segments previously formed, there is produced a chain of segments called a strobila, each segment being known as a proglottid. The proglottids just behind the neck are the youngest; they are at first indistinct and have no differentiation of internal organs. As they are pushed farther and farther from the scolex, the organs progressively develop, so that

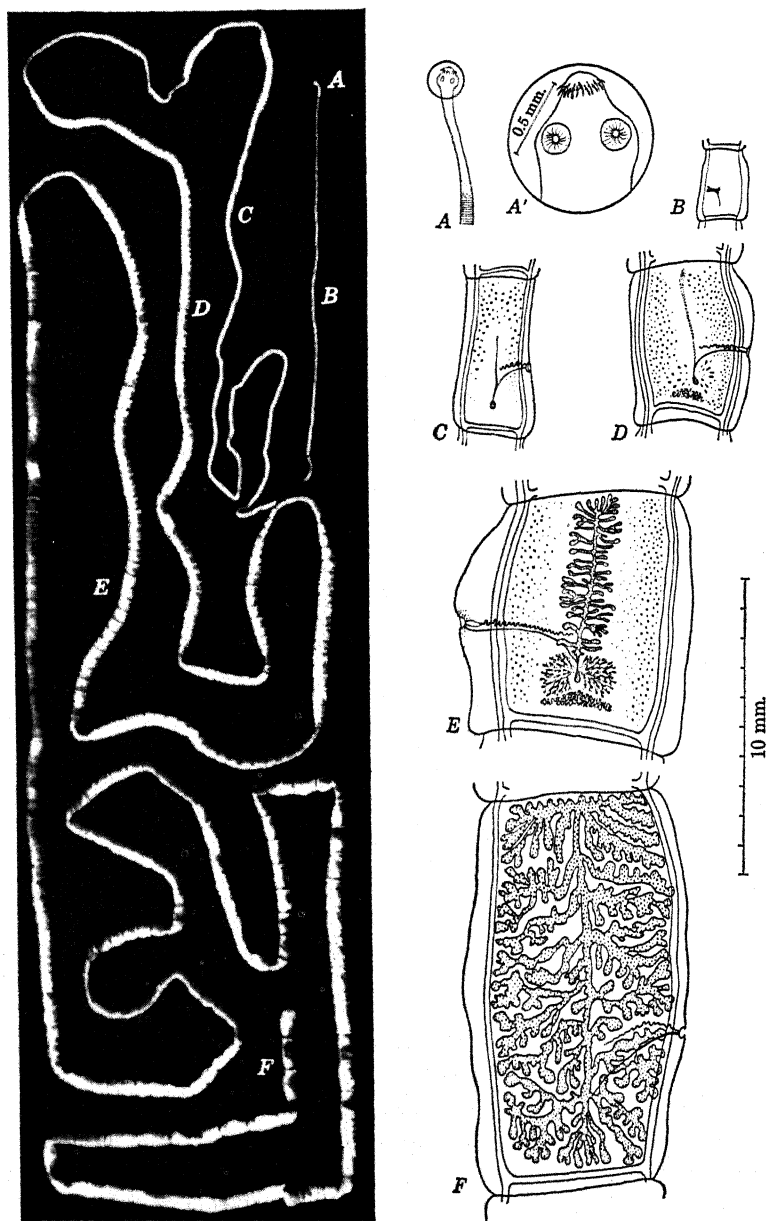


FIG. 86. *Taenia solium*, the pork tapeworm. Left, whole worm, about $\frac{1}{4}$ natural size. Right, enlarged parts of worms from regions indicated on whole worm, showing progressive development of proglottids. In C the testes are just beginning to appear; in D the male system is fully functional, but the female system is immature; in E both systems are fully mature and functional; and in F the ripe uterus has usurped the whole segment, only the vagina and sperm duct being still recognizable.

it is possible to find in a single tapeworm a complete developmental series of proglottids from infancy to old age. The young undifferentiated segments just behind the neck gradually attain sexual maturity in the middle portions of the worm, and then the segments either continue to produce and shed eggs throughout the rest of the strobila (in Pseudophyllidea) or there follows a gradual decadence of the reproductive glands (in Cyclophyllidea) as the segments "go to seed" and become filled by the pregnant uterus with its hordes of eggs (Fig. 86). The whole process can be likened to the development of an undifferentiated bud into a perfect flower and then a seed pod.

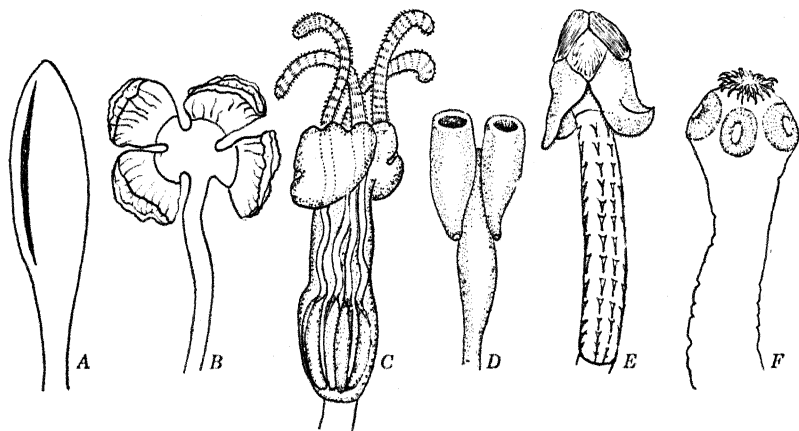


FIG. 87. Types of scoleces of tapeworms. A, order Pseudophyllidea (*Dibothriocephalus latus*); B, order Tetraphyllidea (*Phyllobothrium* sp.); C, order Trypanorhyncha (*Otobothrium* sp.); D, order Pseudophyllidea (*Bothridium* sp.); E, order Diphyllidea (*Echinobothrium* sp.); F, order Cyclophyllidea (*Taenia solium*).

Anatomy. The scolex of a tapeworm serves primarily as an organ of attachment, though it also contains what little brain a tapeworm has. Considering the entire subclass Cestoda, the variety of holdfast organs developed by the scolex is remarkable (Fig. 87), consisting of groove-like, in-cupped, or ear-like suckers, and in addition, in some species, crowns of powerful hooks or rows of spines on a fleshy anterior protuberance called a rostellum, in some forms retractile into a pouch. In one order (Trypanorhyncha) there are long, protrusible, spiny proboscides retractile into canals in the neck (Fig. 87C). The scoleces of the tapeworms infesting mammals, however, are comparatively monotonous in form.

Like flukes, tapeworms are covered by a cuticle secreted by cells underlying it in the spongy mesodermal parenchyma in which all the

other organs are imbedded. The nervous system consists of a few ganglia and commissures in the scolex, from which longitudinal nerve cords run through the length of the worm, the largest ones being a pair near the lateral borders. Coordination of movement is very limited, although the whole worm can contract at once, as when dropped into cold water. Individual ripe segments, when detached, show considerable sensitiveness and are often very active. The excretory system or, preferably, osmoregulatory system, according to Wardle and McLeod (1952), is fundamentally of the same type as in flukes and consists typically of two pairs of lateral longitudinal tubes, the ventral pair usually larger than the dorsal and connected by a transverse tube near the posterior end of each proglottid, and sometimes by a network of smaller tubes. The dorsal vessels carry fluid towards the scolex, the ventral ones away from it. From the ventral vessels extend fine capillaries that end in flame cells. The first-formed proglottid has a terminal bladder as in flukes, but this is lost when this proglottid is cast off, and subsequently the excretory tubes open separately at the end of the last segment still attached. The muscular system consists of longitudinal, transverse, and circular layers of fibers, some just under the cuticle but mostly in a band which encircles the worm at some distance from the cuticle, dividing the parenchyma into cortical and medullary portions. In thick, fleshy species these muscle layers are well developed, whereas in the semitransparent forms they are not.

As of flukes, the main business of tapeworms is the production of myriads of eggs in order to safeguard the species against extermination in the perilous transfer from host to host. Each proglottid possesses complete reproductive systems of both sexes, fully as complete as in the flukes, if not more so (Fig. 88), and in some species each proglottid has a double set of organs.

The female system consists of an ovary, which may be single or in two more or less distinct lobes; yolk glands, either in a single or bilobed mass, or scattered through the segment; Mehlis' glands around an oötype, where the component parts of the egg are assembled; a vagina for the entrance of the sperms, with an enlarged chamber, the seminal receptacle, for storage of sperms; and a uterus, which may or may not have an exit pore. In the tapeworms which have a pore (order Pseudophyllidea), the development and extrusion of eggs goes on continuously in many segments at once, but in the Cyclophyllidea there is no uterine opening. In these the uterus eventually becomes packed with eggs and may practically fill the segment, which is essentially a seed pod. Such "ripe" segments detach themselves from the end of the chain, subsequently liberating their eggs by disintegration, or by

extrusion of the eggs through ruptures during the active contractions and expansions of the segments. The form of the ripe uterus varies greatly in different families, genera, and species, and is often useful in identification (Fig. 89).

The male system consists of a variable number of scattered testes connected by minute tubes with the sperm duct or vas deferens, which

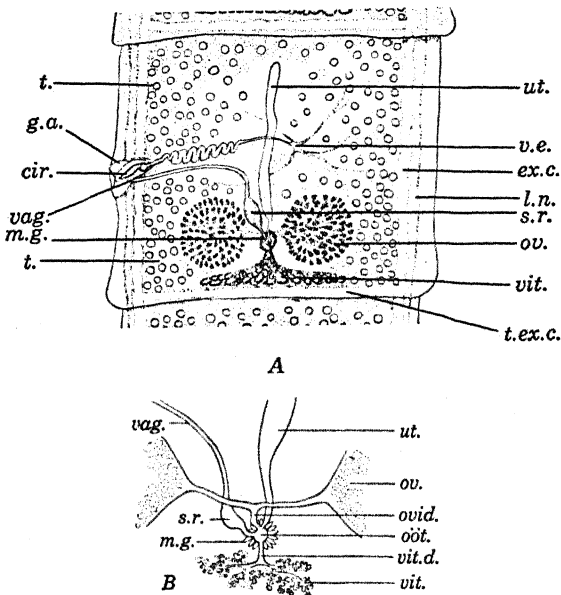


FIG. 88. *Taenia solium*: A, mature proglottid; B, region of oötype; *ex.c.*, excretory canal; *l.n.*, lateral nerve; *oot.*, oötype surrounded by Mehlis' glands; *ov.*, ovary; *s.r.*, seminal receptacle; *t.*, testes; *ut.*, uterus; *vag.*, vagina; *vit.*, vitellaria; *v.d.*, vas deferens. (After Brown, *Synopsis of Medical Parasitology*, 1953.)

is usually convoluted and may have an enlargement, the seminal vesicle, for storage of sperms. The end of the vas deferens is modified into a muscular intromittent organ, the cirrus, which is retractile into a cirrus pouch or sac. In most tapeworms both cirrus and vagina open into a common cup-shaped genital atrium, with a pore on either the lateral border or the mid-ventral surface. Either self-fertilization of a single segment or cross-fertilization between different segments of the same or other worms can occur, but probably fertilization between segments is commonest. As a rule the male reproductive organs mature before the female.

Life Cycle. The life cycle is not quite so complicated as in flukes and does not involve asexual generations, although in some species

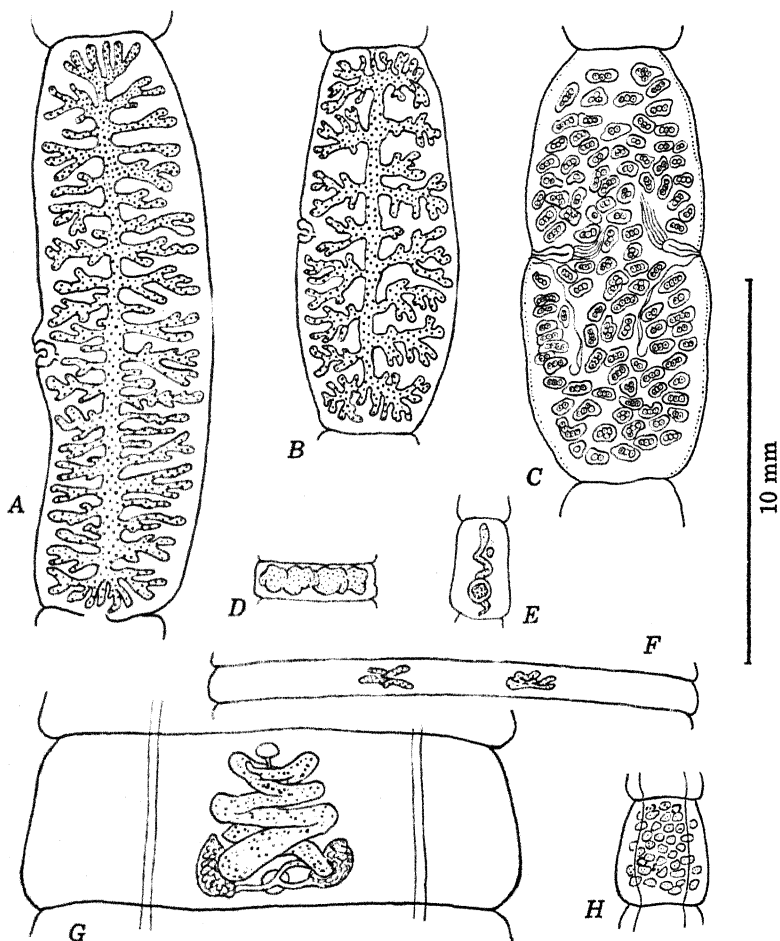


FIG. 89. Ripe proglottids of various tapeworms. A, *Taenia saginata*; B, *T. solium*; C, *Dipylidium caninum*; D, *Hymenolepis diminuta*; E, *Mesocostoides variabilis*; F, *Diplogonoporus grandis*; G, *Dibothriocephalus latus*; H, *Raillietina* sp.

the larval forms multiply by budding. The life cycle of many tapeworms, especially those of fishes, is still unknown; in fact, it was not until the middle of the last century that Küchenmeister proved that the bladderworms in pigs and cattle were in reality the larvae of the common large tapeworms of man; previous to that time they were classified in a separate order, Cystica.

The eggs of tapeworms develop within themselves little spherical embryos characterized by the presence of three pairs of claw-like hooks, whence they are known as oncospheres (Fig. 90A and B). One or two

enclosing membranes inside the egg shell proper form about the developing embryo, the inner one of which is called the embryophore.

In the order Pseudophyllidea the embryos, called coracidia (Fig. 94C), are covered by a ciliated embryophore. They have a brief free-swimming existence, like miracidia, in which they roll about by means of their cilia long enough to attract the attention of copepods which devour them. In these they shed their ciliated covering and change into elongated oval "procercoids" (Fig. 94E, F, G), comparable with

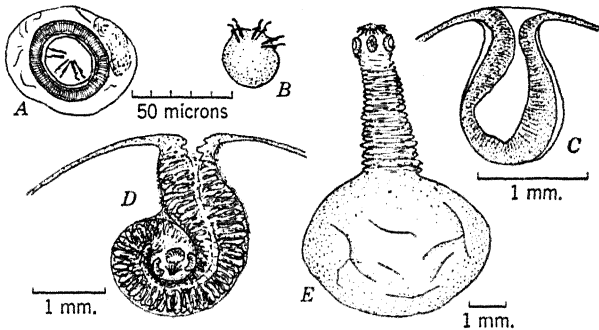


FIG. 90. Stages in life cycle of *Taenia solium*. A, egg containing embryophore; B, hatched oncosphere; C, invagination in wall of developing cysticercus, at bottom of which the scolex will form; D, invagination after development of the scolex; E, cysticercus with head and neck evaginated. (A, B, C, after Blanchard from Brumpt, *Précis de parasitologie*, 1949.)

sporocysts but solid and incapable of asexual reproduction. The six hooks are still present on a small caudal appendage, the cercomer. Further development into a "plerocercoid" (Fig. 96) occurs only when the infected copepod is eaten by a fish or other animal. The plerocercoids are solid worm-like larvae with a scolex invaginated at one end. When the animal containing them is eaten by the final host, the scolex turns right side out and attaches itself to the intestinal wall, and the mature tapeworm develops.

In the order Cyclophyllidea, on the other hand, the oncosphere remains passively in the egg, surrounded by the non-ciliated embryophore until eaten by the intermediate host. Here it transforms into a bladder-like structure, a part of the wall of which differentiates into one or more scoleces turned inside out (invaginated) (Fig. 90C and D). Sometimes the whole embryo becomes hollow and grows into a large bladder, into the spacious cavity of which the relatively small scolex or scoleces are invaginated; such a larva is called a *cysticercus* or bladder-worm if there is only one scolex, and a *coenurus* (Fig. 100) if there are a number of them. In one tapeworm, *Echinococcus*, the bladders add

a further method of multiplication by budding off daughter and grand-daughter bladders, and the bladder walls, instead of directly producing scoleces, first produce brood-capsules, each of which in turn produces on its wall a number of scoleces, whereby one huge larval cyst, called a *hydatid*, may be the mother of many thousands of tapeworms (Figs. 102, 103). Sometimes the main portion of the body of the embryo remains solid and grows very little, while one end of it becomes hollowed out into a small bladder containing the invaginated scolex (Figs. 104, 105). The undeveloped solid portion remains as a caudal appendage. Such a larva, called a *cysticercoid*, is characteristic of those tapeworms which use arthropods as intermediate hosts.

On being eaten by a final host only the scoleces survive; these turn right side out (evaginate), attach themselves to the mucous membrane of the intestine, and grow each into a mature tapeworm. In one progressive genus, *Hymenolepis*, a few species have broken away from the traditional intermediate host idea and may complete their development in one host; the cysticercoids develop inside the intestinal villi and subsequently gain the lumen of the intestine where the mature phase is attained. For a long time parasitologists were very skeptical of the truth of such unorthodoxy on nature's part.

Classification. The classification of the Cestoidea is much more satisfactorily worked out than that of the Trematoda. There are two subclasses, Cestodaria and Cestoda. The Cestodaria do not form segments, having a single set of reproductive organs; the vagina and male genital opening are near the posterior end; and the embryos have ten or twelve hooks (Fig. 91B). This subclass contains two orders. The Amphiliniidea (Fig. 91C) are parasitic in the celom of fishes or (in one species) a fresh-water turtle, and use amphipods as first intermediate hosts; they are probably neotenic, i.e., precociously mature larvae (plerocercoids) in the second intermediate host, the true definitive hosts having been abandoned. The Gyrocotylidea (Fig. 91A), parasitic in the primitive chimaeroid fishes, appear to develop like the monogenetic trematodes, without bothering with an intermediate host. The Cestoda, which alone concern us here, produce reduplicated reproductive organs, usually in distinctly demarcated segments or proglottids, except in one order, Caryophyllidea, which in other anatomical characters resembles the Pseudophyllidea. The Cestoda have a well-developed scolex, genital openings anterior to the ovary, and embryos with only six hooks.

The cestodes are an ancient group which probably evolved with the sharks and rays; four of the eleven orders are still confined to them. It is not surprising that there are a number of aberrant forms which have

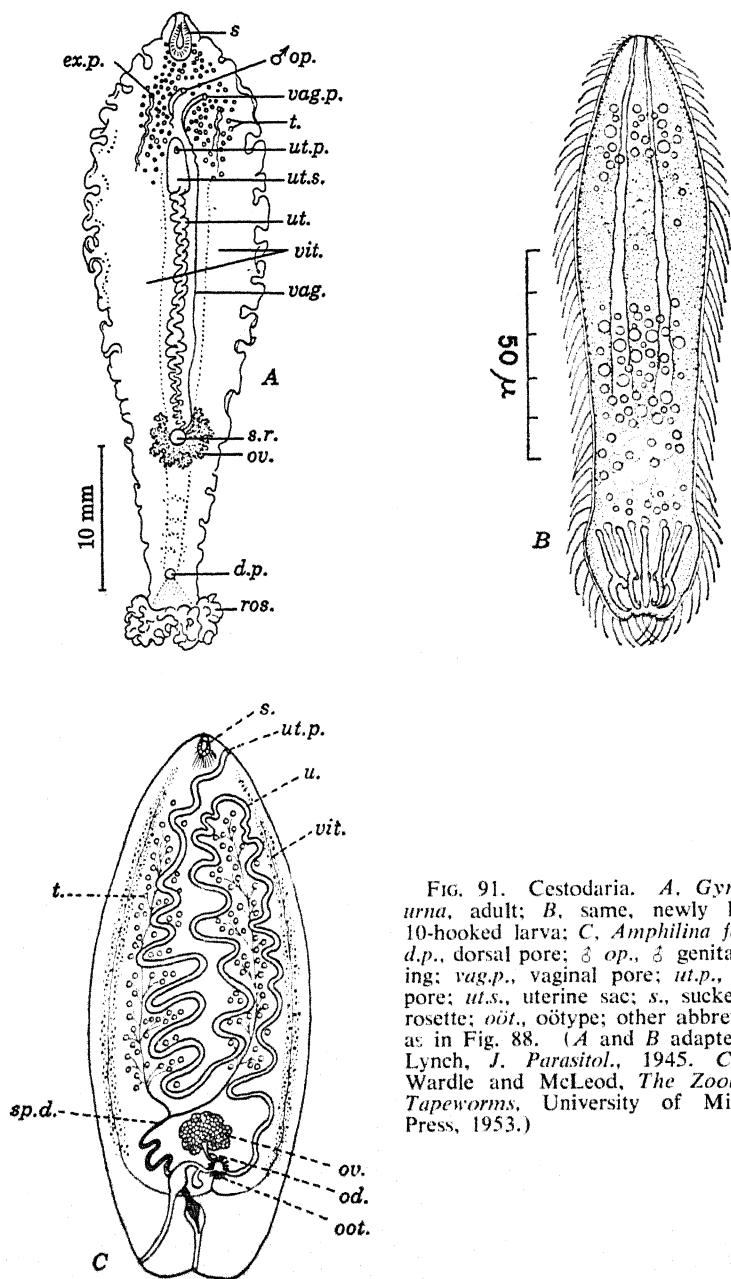


FIG. 91. Cestodaria. A, *Gyrocotyle urna*, adult; B, same, newly hatched 10-hooked larva; C, *Amphilina foliacea*; *d.p.*, dorsal pore; *♂ op.*, ♂ genital opening; *vag.p.*, vaginal pore; *ut.p.*, uterine pore; *ut.s.*, uterine sac; *s.*, sucker; *ros.*, rosette; *oot.*, oötype; other abbreviations as in Fig. 88. (A and B adapted from Lynch, *J. Parasitol.*, 1945. C, after Wardle and McLeod, *The Zoology of Tapeworms*, University of Minnesota Press, 1953.)

no near relatives, and which do not fit into any of the large groups. Wardle and McLeod (1952) recognize eleven orders, but only five of these contain numerous forms; the others contain only a few each, one only a single species. The Tetraphyllidea, with numerous and varied forms in elasmobranchs, represent a sort of central stock from which in the more or less distant past all the other orders have evolved; the Trypanorhyncha, with their remarkable spiny proboscides, remained in elasmobranchs; the Pseudophyllidea switched to bony fishes, and some eventually to animals feeding on bony fishes; the Proteocephala explored the possibilities of parasitizing fresh-water vertebrates from fishes to reptiles, and with the advent of birds and mammals onto the scene were probably the group from which came the Cyclophyllidea, the dominant group in these animals. Following are the principal orders and their characters:

1. Order **Tetraphyllidea**. Head with four ear-like or lappet-like outgrowths (bothridia) (Fig. 87B); proglottids in various stages of development; vitelline glands scattered in two lateral rows or bands; genital pores lateral. In Elasmobranchs.

2. Order **Trypanorhyncha**. Head with two or four bothridia and four long evertible proboscides armed with hooks or spines, retractile into sheaths (Fig. 87C); yolk glands in continuous sleeve-like distribution. In elasmobranchs.

3. Order **Pseudophyllidea**. Head with two lateral or, rarely, one terminal, sucking grooves (bothria) (Fig. 87A and D); majority of proglottids in similar stage of development, shedding eggs from a uterine pore; genital pores mid-ventral; vitelline glands scattered in dorsal and ventral sheets. In teleosts and land vertebrates.

4. Order **Proteocephala**. Head with four in-cupped muscular suckers, and sometimes a fifth terminal one; genital pores lateral; vitelline glands in lateral bands; uterus with one or more median ventral openings made by breaks or clefts in the body wall. In fresh-water fishes, amphibians, and reptiles (except one in a shark).

5. Order **Cyclophyllidea**. Head with four in-cupped suckers (Fig. 87F); proglottids in all stages of development, ripe ones only near end of chain; no uterine pore; genital pores usually lateral; vitelline gland a single or bilobed mass posterior to ovary. Majority in birds and mammals.

Only the Pseudophyllidea and Cyclophyllidea contain species which attack man or domestic animals. Although 25 or 30 different species of tapeworms have been recorded in man, only 4 adult species and 3 larval species are at all common. The order Pseudophyllidea contains one in each group, *Dibothriocephalus latus* as an adult, and *Spirometra mansoni* as a larva; the order Cyclophyllidea includes as adults *Taenia solium*, *T. saginata*, and *Hymenolepis nana*, and as larvae *T. solium* and *Echinococcus granulosus*. *H. diminuta* and *Dipylidium caninum* are much less rare than the records indicate, but all the others, some of which are briefly described in the following pages, are rare.

Most tapeworms are astonishingly particular about their hosts. They undergo evolution more slowly than the hosts and therefore stick with them, unchanged even after the hosts have evolved into genera and species which may now be separated by oceans and continents. The tapeworms harbored by a bird may be a better indication of its phylogenetic affinities than some of its anatomical characters; in several instances tapeworms have proved more reliable than ornithologists in showing the relationships of birds.

Diagnosis. Tapeworms cannot invariably be diagnosed by examining feces for eggs. The pseudophyllidean tapeworms can be diagnosed in this way, since the operculated eggs are expelled through the uterine pores of many proglottids at a time and are therefore always present in the feces. Like the eggs of flukes, these eggs do not float in saturated salt solution; they can be concentrated by straining and sedimenting or centrifuging in water, or by the AMS III method (see p. 255). *Hymenolepis* infections can also be diagnosed by fecal examination for eggs, even though no birthpore is present, since the segments broken off from the ends of the worms commonly rupture before leaving the body of the host; *Hymenolepis* eggs are easily found by flotation methods. In *H. nana* the partitions between ripe segments break down before the segments are shed, permitting the eggs from several segments to escape from the end of the worm.

Taenia and many other tapeworm infections cannot be reliably diagnosed in this manner, since the segments often escape from the body uninjured and still alive. Search must be made for the voided segments in the stools; the shape of the segment and form of the gravid uterus serve to identify the species. *Taenia* eggs are present in the feces only when segments rupture; those of *T. saginata* can usually be found on the perianal skin, like those of *Enterobius* (see p. 451). The thick, striated embryophores are porous and therefore cannot be found by flotation.

The eggs of *Dibothriocephalus* (Fig. 57L) may be confused with those of flukes, but they are different in size from any common human fluke eggs (60 to 70 μ). All other tapeworm eggs of man are recognizable as such by their six-hooked embryos. *Taenia* and *Hymenolepis* eggs (Fig. 57N, O, and P) cannot be confused when one has once seen them, but many inexperienced physicians, unfamiliar with *Hymenolepis*, take all eggs with six-hooked embryos to be *Taenia*, sometimes with disconcerting results. A physician who found tapeworm eggs in the stool of a high-class Indian Brahmin mortally offended him by telling him he had eaten insufficiently cooked beef or pork, when in reality the eggs were those of *Hymenolepis*.

Treatment. For the most part the drugs most useful in expelling tapeworms constitute a group distinct from those effective against nematodes, although carbon tetrachloride and hexylresorcinol have some effectiveness against both groups of worms. Tapeworms are affected by a number of drugs of vegetable origin—filix mas, Cusso, Kamala, pelletierine, arecoline hydrobromide—which have not been found effective against other helminths. Ethereal extract of *Aspidium* (filix mas or male fern) was the standard drug for expelling tapeworms from man for many years, and arecoline hydrobromide is still most extensively used for dogs.

An acridine compound (Acranil), related to atebirin, was first used against tapeworms by Neghme in Chile in 1938, and atebirin by Culbertson shortly after. Atebrin has now largely replaced *Aspidium* for human tapeworm infections. The usually recommended dose of atebirin for adults is eight to ten 0.1-gram tablets in a single dose—two tablets every 5 minutes. This usually clears 60 to 90 per cent of *Taenia* cases in one treatment. It cures 40 to 75 per cent of *Hymenolepis nana* infections, in all cases removing a high percentage of the worms; in one case reported by Beaver and Sodeman 6000 worms were passed. Neghme and Bertin (1951) found atebirin successful in removing *Dibothriocephalus latus* in all cases tried. The drug is given on an empty stomach in the morning, and followed in 2 to 4 hours by a strong saline purge. Chloroquine seems to be a little less effective than atebirin. Introduction of 0.8 gram of atebirin in 100 cc. of water behind the stomach by duodenal tube is an even more effective treatment; it expelled *all* worms from patients who didn't interfere with the treatment by vomiting, which was done more frequently by women. Treatment for species of *Taenia* should not be repeated until segments or eggs again appear in the feces, for sometimes the scoleces are not easily seen when passed. The worms are more easily expelled when there is a considerable length of paralyzed worm to drag on the scolex.

German workers (see Kuhls, 1953) have recently revived the use of tin as an anthelmintic for tapeworms. Tablets containing a mixture of metallic tin, tin oxide, and zinc chloride, given before meals and with no following purge, are reported to be highly effective (90 per cent cures) and non-toxic.

Prevention. Prevention varies, of course, with the species of tapeworm and its intermediate host. But since infection with the common human species, with the exception of the species of *Hymenolepis*, results from eating raw or imperfectly cooked beef, pork, or fish in which the larvae have developed, the exclusive use of thoroughly cooked meat and fish is the best preventive measure. Pork and beef bladderworms

are killed when heated to 55°C., but it is difficult to heat the center of a large piece of meat even to this point; a ham cooked by boiling for two hours may reach a temperature of only 46°C. in the center. When roasted, pork should always be cut into pieces weighing no more than three or four pounds to insure thorough penetration of heat. Beef which has lost its red or "rare" color is quite safe. At 0° to 2°C. the cysticerci of *T. solium* live for over 50 days, but at -5°C. they die in about a week. Quick-freezing is destructive to cysticerci, as is thorough curing or salting of meat. The meat of sheep, goats, or chickens does not convey any parasites to man, even if uncooked.

Prevention of cysticercus infections in cattle or pigs depends on care to prevent contamination of the animals' water or food by human feces. Eggs of *Taenia saginata* may live in liquid manure for over 10 weeks and on contaminated grass, if not allowed to dry, for over 20 weeks.

The dwarf tapeworm, *H. nana*, and those which develop in arthropods are subject to different means of prevention (see p. 364). No effective method of protection of herbivores against anoplocephalid tapeworms, which utilize free-living mites as intermediate hosts, has yet been devised.

Order Pseudophyllidea

All the members of the Pseudophyllidea which live in man or domestic mammals are members of the family Diphyllbothriidae. These are large worms consisting of long chains of numerous segments and a head provided with a slit-like groove or bothrium on either side. The majority of the segments are mature and functional at one time and deposit eggs through the uterine pores as more are being developed. Eventually, as old age overtakes them, the proglottids cease to produce more eggs; they gradually empty their uteri and then, shrunken and twisted, are sloughed off in long chains. The general type of life cycle, involving a copepod as a first intermediate host and a vertebrate as a second, has already been described on p. 335.

There are about 75 species in the family, living in whales, porpoises, seals, sea lions, fish-eating land carnivores, fish-eating birds, and man. All of these, except a few bird tapeworms that have indistinct or no external demarcation of the segments (*Ligula* and *Schistocephalus*), have been commonly lumped together in the genus *Diphyllbothrium*. Since several well-defined groups occur, with quite well-marked characters, it has become desirable to break up this large group into several genera. Wardle, McLeod, and Stewart (1947) recognized seven genera, five of them parasitic in marine mammals. The species which commonly lives as an adult in man falls into the genus *Dibothriocephalus*,

which was created for it before this and all the other species were merged into the genus *Diphyllbothrium*. The latter genus was first erected for a large species with a small oval head and no obvious neck, found in porpoises.

The genus *Dibothriocephalus* (not to be confused with *Bothriocephalus*, which has both its plerocercoid and adult stages in fishes) contains the human species, *D. latus*, and several others reported from fish-eating mammals and birds. They are large, slender, weakly muscular forms with an elongated, compressed scolex with slit-like grooves or

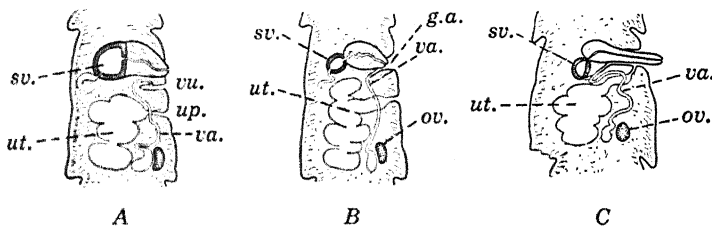


FIG. 92. Arrangement of organs of various genera in the family Diphyllbothriidae as seen in sagittal sections. A, *Spirometra*, with separate openings for cirrus, vagina, and uterus; B, *Dibothriocephalus*, with common opening for cirrus and vagina; C, *Pyramicocephalus*, with common opening for cirrus, vagina, and uterus. Abbreviations: g.a., genital atrium; ov., ovary; s.v., seminal vesicle; u.p., uterine pore; ut., uterus; va., vagina; vu., vulva. (After Mueller, *J. Parasitol.*, 22, 1936.)

"bothria" which are narrow and deep; a long slender neck; a rosette-shaped uterus; a common opening for cirrus and vagina (Fig. 92B); eggs rounded at the ends; and plerocercoids in fish. A closely related genus, *Spirometra*, contains smaller and weaker worms, found primarily in cats, which have broader and shallower bothria; a uterus with a spiral of close coils; separate openings for cirrus and vagina (Fig. 92A); eggs pointed at the ends; and plerocercoids usually in frogs, snakes, birds, or rodents. Some, possibly all, of this group can live in human flesh in the plerocercoid or "sparganum" stage, causing sparganosis. One species, *S. houghtoni*, has been recorded a few times as an adult from a man in China.

There are a few records of human infection with other adult diphyllbothriids, normally found in marine carnivores, and also with worms of the genus *Ligula*. This and the related *Schistocephalus* reach a large size before being transferred from fish to their normal bird hosts. Smyth (1947) was able to get the plerocercoids to mature their reproductive organs in artificial media at 40°C.

Morphology. The arrangement of the organs in mature proglottids of a diphyllbothriid is shown in Figs. 93 and 97. The female system

consists of a vagina opening on the mid-ventral surface in the anterior part of the segment and running almost straight posteriorly to an oötype surrounded by a Mehlis gland. The ovaries are paired in the posterior part of the segment. The yolk glands are scattered throughout the lateral fields. The uterus has an inner series of delicate coils as it leaves the oötype, followed by an outer series of large coarse ones. The uterine opening is on the ventral surface but is inconspicuous. The male system consists of a large number of testes scattered in the lateral fields, largely obscured by the vitelline glands which lie dorsal and ventral to them. The cirrus and cirrus pouch are anteriorly situated.

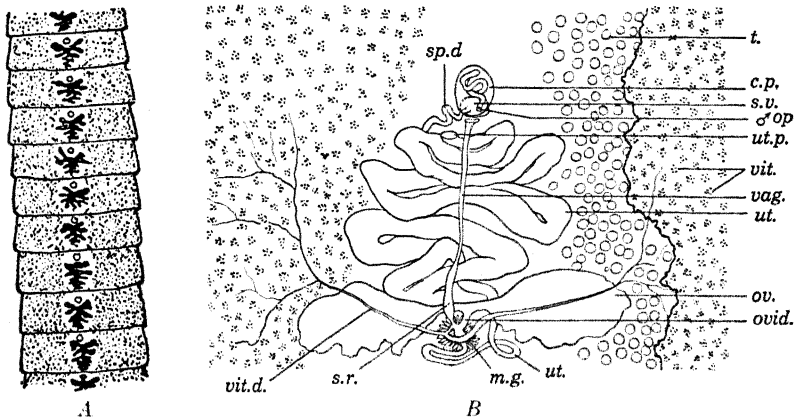


FIG. 93. *Dibothriocephalus latus*. A, chain of proglottids, natural size. B, middle portion of proglottid; c.p., cirrus pouch; M.g., Mehlis' gland; ♂ op., male genital opening; ov., ovary; ovid., oviduct; sp.d., sperm duct; s.r., seminal receptacle; s.v., seminal vesicle; ut., uterus; vag., vagina; vit., vitellaria; vit.d., vitelline duct. Superficial layer cut away on right to expose testes.

***Dibothriocephalus latus*.** This worm, possibly constituting a group of nearly related species, is called the "broad" or "fish" tapeworm. It is the largest tapeworm found in man. It has long been known in many parts of central Europe; in Finland about 20 per cent of the population harbor this worm, and in some local areas in the Baltics nearly 100 per cent are infested. The worm also occurs in Ireland, Siberia, Palestine, Japan, Central Africa, Chile, and in Michigan, Minnesota, Wyoming, Manitoba, Alaska, and Florida in North America. It has been thought that the worm was introduced into North America by Scandinavian lumbermen, but it may also have entered by the Bering Straits, or there may have been a native species in our wild carnivores before European or Asian man or dogs arrived. Worms from Manitoba and from Russia look different, but there is so much variation

in different parts of a worm, in worms of different ages and in different hosts, and in worms differently prepared, that no specifically differential characters have been found.

D. latus reaches maturity in many domestic and wild species of the dog and cat families, in bears, and possibly other fish-eating carnivores. In North America the brown bear may be the normal host; dogs may not be as important since many of the eggs passed by them are not viable.

D. latus is a veritable monster, reaching a length of 10 to more than 30 ft., with a width of 10 to 12 or even up to 20 mm., and with a total of 3000 to 4000 proglottids in large specimens. Tarassov tells of a Russian woman who harbored six worms, aggregating over 290 ft., and of another who supported 143 worms. Fortunately in tapeworm infections the size of the worms usually is in inverse proportion to their number. The proglottids (Fig. 93) for the most part are much broader than long, although the terminal ones become approximately square.

LIFE CYCLE. The broadly oval, operculated eggs, which average about 60 by 42 μ , contain abundant yolk cells (Fig. 57L). Ciliated embryos, or coracidia, develop slowly in the eggs, hatching after 8 or 10 days to several weeks, depending on temperature. The coracidia (Fig. 94C), 50 to 55 μ in diameter, swim by means of their cilia or creep on the bottom after slipping out of their ciliated coverings, but they must be eaten by certain species of copepods (Fig. 94D) in less than 24 hours if they are to continue their development and fulfill their destiny.

The worm is very fastidious about its first intermediate hosts, and in America develops only in certain species of the genus *Diaptomus* (distinguished by having very long first antennae), which live in the open water of lakes. Many species of *Diaptomus* are known to serve as hosts, but other copepods do not, although species of *Cyclops* are the preferred hosts of *Spirometra*.

Soon after the coracidium is ingested by a copepod it loses its ciliated covering, and the naked oncosphere, only 24 μ in diameter, bores through into the body cavity. In 14 to 18 days it develops into a solid, elongate creature. The embryonic hooks persist in a bulb-like appendage, the cercomer, which is partially pinched off at the posterior end, and eventually discarded; a cup-shaped depression, into which histolytic glands open, appears at the anterior end; some species also have spines at the anterior end. The worm is now a procercoïd, about 500 μ long (Fig. 94D, G).

Further development occurs in fish when the infected copepod is eaten. The passage through the intestine and body cavity of the fish is slow, but eventually the larvae reach the flesh of the fish and grow

into elongated worm-like plerocercoid larvae, 4 or 5 mm. to several centimeters in length. They are not encysted and are found anywhere in the flesh, in other places only rarely. In this respect *D. latus* differs from some of the related species that develop in birds, since the latter are found encysted on the mesenteries in the abdominal cavity or in the

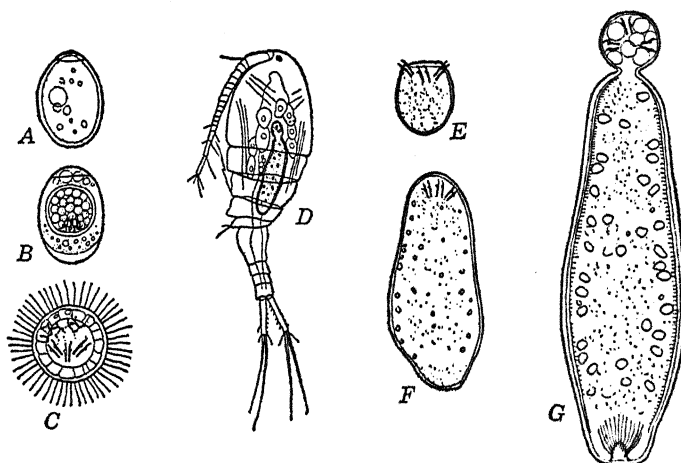


FIG. 94. Developmental stages of *Dibothriocephalus latus*: A, undeveloped egg; B, egg containing developed embryo; C, free embryo or coracidium; D, *Cyclops strenuus* containing procercoid; E, embryo after shedding ciliated envelope in *Cyclops*; F, growing procercoid; G, full grown procercoid. (After Brumpt, *Précis de parasitologie*, Masson, 1949.)

liver. The smaller plerocercoids lie straight, but with growth they become increasingly bent and twisted (Fig. 95). The anterior end has a depression which is the withdrawn and inverted scolex; the remainder of the body is white, somewhat flattened, and marked by irregular wrinkles, but without segmentation. In uncooked fish their opaque white color shows clearly through the translucent flesh, but cysts of flukes or other tapeworms may be confused with them if they are not carefully examined. Cysts of tapeworms of the genus *Proteocephalus* are often present, but these have four or five cup-shaped suckers on the head; the elongate but cramped plerocercoids abundant in tullibee (*Leuciscus*) in some lakes in northern United States are readily distinguished by the tridents on the head; some of the other plerocercoids found in herring, perch, trout, etc., are more difficult to distinguish. Drum, gulf "trout," etc., from the Texas coast frequently contain the very elongate "spaghetti worm" plerocercoids of *Trypanorhynchus*, which mature in sharks and rays. None of these become human parasites.

The fish that serve as second intermediate hosts of *Dibothriocephalus latus* are carnivorous species, but they seem to differ in different localities. In northern United States and Canada pike and walleyes (*Esox* and *Stizostedion*, Fig. 95D and E, are by far the most important hosts; in northern Europe, trout, perch, and burbot; in Lake Baikal, species of *Coregonus* and *Thymallus*; in Chile and in the Far East, trout (*Oncorhynchus* and *Salmo*); and in Africa, the barbel (*Barbus*).

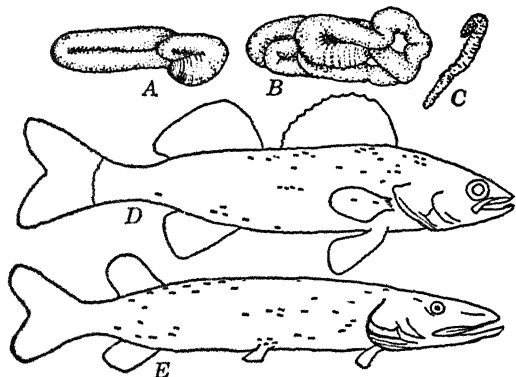


FIG. 95. A to C, plerocercoid larvae of *D. latus* as they appear in the flesh of fishes, $\times 3$; D, wall-eyed pike (*Stizostedion*) showing distribution of 35 plerocercoids in the flesh; E, northern pike (*Esox lucius*) with 37 plerocercoids. (After Vergeer, *J. Inf. Dis.*, 44, 1929.)

In some small lakes in northern United States and Canada 50 to 75 per cent of the pike and walleyes harbor larvae of this worm. These large carnivorous fish do not feed intentionally on copepods and probably ingest them in the stomachs of smaller fish on which they prey. It is a peculiarity of plerocercoid larvae that they are able to reinvade and become re-established in host after host until one is reached in which maturity can be attained in the intestine. Those of *D. latus* can pass from fish to fish, and those of *Spirometra* may be passed about among frogs, reptiles, and mammals.

Infection of the final host comes from eating imperfectly cooked flesh or roe of infected fish or from conveying small plerocercoids to the mouth by the hands, to which they cling while fish is being cleaned. In 3 weeks they may have reached a length of 3 ft. and may begin producing eggs in that time. It has been estimated that one worm produces 36,000 eggs daily. In northern United States many towns pour their sewage directly into lakes, and the inhabitants fish for pike, which harbor the plerocercoids, near the sewage outlets. Summer visitors in camps and hotels often partake of fish hastily prepared,

content with a well-done exterior. Dogs and cats are usually given the raw refuse and help to keep the infection alive. Furthermore, millions of pounds of walleyes and pike are annually imported from infected Canadian lakes for the preparation of "gefüllte fish." Many cases develop among Jewish people, presumably as a result of tasting the fish during the preparation, before it is cooked.

PATHOLOGICAL EFFECTS AND TREATMENT. Common effects of *D. latus* infection are abdominal pain, loss of weight, and progressive weakness, similar to the symptoms of *Taenia* infections (see p. 355). This worm is, however, unique among tapeworms in sometimes causing a very severe anemia of the pernicious type. Fortunately, this severe anemia is the exception rather than the rule. In Finland, although the Finlanders are said to be more prone to pernicious anemia than other races, the anemia rate is only 5 to 10 per 10,000 infections. It was once thought that the anemia was produced by a toxic effect, but the writer (Chandler, 1943) suggested absorption of a vitamin-like substance by the worms as a possible explanation. Subsequently it became known that vitamin B₁₂ plays an important role in blood formation. Work by von Bonnsdorf (1952) and by Nyberg (1952) demonstrated that *D. latus* does actively soak up vitamin B₁₂, absorbing ten to fifty times as much as other tapeworms, and in fact becomes so rich in it that administration of powdered worms along with gastric juice is as effective in curing pernicious anemia as is administration of vitamin B₁₂.

CONTROL. Control of *D. latus* infection must depend mainly on more careful cooking of fish. Housewives and cooks preparing "gefüllte fish" should refrain from tasting the raw fish to test their skill in flavoring. Some reduction in the infection of fish could be obtained by education and regulation with respect to pollution of lakes, and the practice of feeding raw fish to dogs and cats should be discouraged.

"Sparganum" Infections. The plerocercoid larvae of worms of the genus *Spirometra*, for which the name *Sparganum* was given before their adult forms were definitely known, normally develop in frogs, snakes, or amphibious mammals, but when opportunity is afforded can live in man. The first intermediate hosts are *Cyclops*, which abound in shallow water. Galliard and Ngu (1946) showed that *S. mansoni* in Indo-China apparently requires four hosts, the procercoids from *Cyclops* first infecting tadpoles, and later becoming fully developed plerocercoids when these are eaten by frogs, reptiles, or mammals. This recalls the use of minnows as an intermediate step between *Diaptomus* and carnivorous fish by *Dibothriocephalus latus*.

The larval worm as found in man, usually referred to as *Sparganum mansoni*, is a typical plerocercoid, much larger than that of *D. latus*,

being 3 to 14 in. in length (Fig. 96). It is a whitish, elastic, wrinkled worm with an invaginated scolex at the broader end. In man it is found in the muscles, subcutaneous connective tissue, or around the eye. The largest number of cases have been recorded from Indo-China, China, and Japan, but scattered cases of this or closely related larvae are known from almost every part of the world. In the Orient, human infection is acquired in a remarkable manner; split fresh frogs are commonly used by the natives as a poultice for sore eyes and wounds, and the spargana then transfer themselves to human flesh. Applied to the eye, they may settle in the lids or go to other parts of the face; they are easier to remove after being encapsulated. As noted on p. 346,



FIG. 96. *Sparganum mansonii*, natural size. (After Ijima and Murata, *Coll. Sci. Imp. Univ. Japan*, 2, 1888.)

spargana are able, when eaten by a host which is not suitable for adult development, to reinvade and become encapsulated over again, ready for another try. The range of hosts in which they can become re-established after development is much larger than that in which they can develop originally.

There is much confusion about the species of *Spirometra*, all of which are primarily cat and dog parasites when mature. Wardle and McLeod (1952) list seventeen species which have been described from all parts of the world. There is no way of distinguishing the spargana, and the adult morphology, as in the genus *Dibothriocephalus*, does not lend itself to easy differentiation of species. Some spargana develop only in frogs, some in mice but not in frogs, and some in both. After becoming spargana, however, some species, at least, will re-establish themselves in fish, frogs, snakes, mice, or men—whatever eats them.

It is probable that any species of *Sparganum* of the *Spirometra* group could establish itself in man if swallowed, but it is improbable that the swallowing of infected copepods would result in infection. A few cases of *Sparganum* infection have been recorded in the United States, but there is no information as to the species to which they belong. *Spirometra mansonioides* (Fig. 97) has a wide distribution in wild and feral cats in eastern United States and Texas, and uses wild species of mice for development of the spargana. Mueller and Coulston (1941) showed that when the young spargana of this species are experimentally implanted in human flesh they grow normally; they thought human

cases might be commoner than records indicate and that cysts or fatty tumors removed from under the skin should be suspected.

A few cases have been recorded in which the spargana apparently multiply in the body. Thousands of worms, usually only 3 to 12 mm. in length but sometimes larger, may be present in acne-like nodules in the skin and elsewhere in the body. They apparently proliferate by formation of bud-like growths. This so-called *Sparganum proliferum*

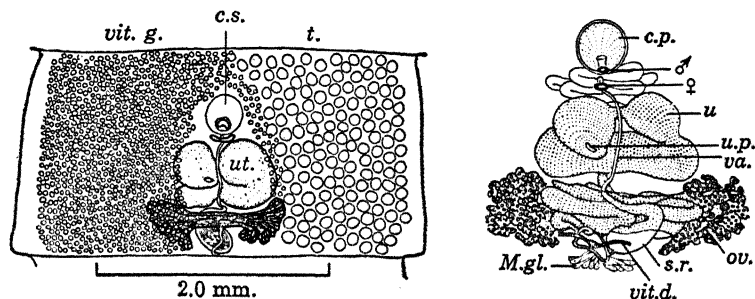


FIG. 97. *Spirometra mansonioides*. Left, young mature proglottid; c.s., cirrus sac or pouch; t., testes; ut., uterus; vit.g., vitelline glands. Right, reproductive organs: ♂ and ♀, genital openings; c.p., cirrus pouch; M.gl., Mehlis' gland; ov., ovary; s.r., seminal receptacle; u., uterus; ut.p., uterine pore; vit.d., vitelline duct. (After Mueller, *Parasitol.*, 21, 1935.)

is now believed to be an abnormal growth in an unfavorable host; it has been found only in man. Mueller (1938), from a careful restudy of specimens of *S. proliferum*, concluded that they are abnormal, degenerate forms without scoleces and without normal orientation of parts.

Order Cyclophyllidea

The vast majority of the tapeworms of mammals and birds belong to the order Cyclophyllidea. These, as noted on p. 338, are distinguished by the presence of four in-cupped muscular suckers on the scolex and often a rostellum armed with hooks, by having the yolk glands concentrated into a single or bilobed mass near the ovary, and by having no uterine pore. The embryos remain passively in the egg or embryophore until eaten by the host in which they are to develop; this may be either a vertebrate or an invertebrate. Reid in 1947 showed that they are provided with a pair of unicellular glands opening between the hooklets and probably helpful in penetration. The larva may be either a cysticercus, a coenurus, a hydatid, or a cysticercoid (see pp. 335-336).

Six families contain species which are habitually or accidentally parasitic in man. These are:

- ✓ **Taeniidae.** Medium-sized or large worms, except *Echinococcus*, which is very small. Scolex usually armed with a double row of large hooks but unarmed in *T. saginata*; ripe uterus with a central stem and lateral branches; genital pores lateral on alternating sides; ovaries and yolk gland in posterior part of segment; testes numerous; eggs with thick, striated inner shells. Important genera in man or domestic animals: *Taenia*, *Multiceps*, *Echinococcus*.
- ✓ **Hymenolepididae.** Medium-sized or small worms, segments usually broader than long; scolex usually with a single row of hooks, but unarmed in *H. diminuta*; ripe uterus sac-like, not breaking up into egg balls; genital pores lateral, usually all on one side; ovary and yolk gland near center of proglottid, and with 1 to 4 testes. Important genus: *Hymenolepis*.
- ✓ **Dilepididae.** Medium-sized or small worms; rostellum usually well-developed, retractile into a rostellar sac, and with 1 to 6 or 8 rows of rose-thorn hooks; genitalia single or double; genital pores unilateral or alternating; testes numerous; ripe uterus a transverse sac (subfamily Dilepidinae), or replaced by a paruterine organ (subfamily Paruterininae), or by egg capsules containing one to several eggs (subfamily Dipylidiinae). Important genus: *Dipylidium*.
- ✓ **Davaineidae.** Medium-sized or small worms. Scolex with a double row of minute hammer-shaped hooks on rostellum and usually with numerous minute hooklets on the margins of suckers; ovaries and yolk gland near center of segment; uterus breaks up into egg capsules; testes fairly numerous. Important genera: *Davainea*, *Railiictina*.
- ✓ **Anoplocephalidae.** Medium-sized or large worms of herbivorous animals. Scolex unarmed; female genital organs single or double in each segment, situated laterally or near middle; testes numerous; uterus develops a transverse sac or tubular network, in subfamily Thysanosominae later developing paruterine pouches; eggs usually with a pair of horn-like processes (*pyriform apparatus*) on one side of inner shell; cysticeroids, as far as known, develop in oribatid mites. Important genera: *Moniezia*, *Anoplocephala*, *Thysanosoma*, *Bertiella*.
- ✓ **Linstowiidae** (formerly included as a subfamily of Anoplocephalidae). Medium-sized or small worms of insectivorous animals; scolex unarmed; sex glands in middle or anterior part of mature segments; testes numerous; uterus breaks down into egg capsules containing one or several eggs; eggs without pyriform apparatus; cysticeroids as far as known develop in beetles. Important genera: *Inermicapsifer*, *Oochoristica*.
- ✓ **Mesocestoididae.** Medium-sized or large worms of carnivorous birds and mammals. Scolex unarmed; genital pore on mid-ventral surface; ripe uterus with or without a paruterine organ; ovaries and yolk glands posterior; testes numerous. Two genera: *Mesocestoides* and *Mesogyna*.

TAENIIDAE

The family Taeniidae includes for the most part relatively large worms parasitic in mammals. The form of the hooks in the armed species is shown in Fig. 98B and the arrangement of organs in the proglottids in Fig. 88. The eggs (Figs. 57P and 90A) have a very thin outer shell, sometimes provided with a pair of delicate filaments, which

is ordinarily lost before the eggs are found in the feces. The inner embryophore has a thick, porous brown shell which on surface view looks honeycombed and in optical section looks striated. The larvae of most species are cysticerci, but in the genus *Multiceps* it is a coenurus and in *Echinococcus* a hydatid.

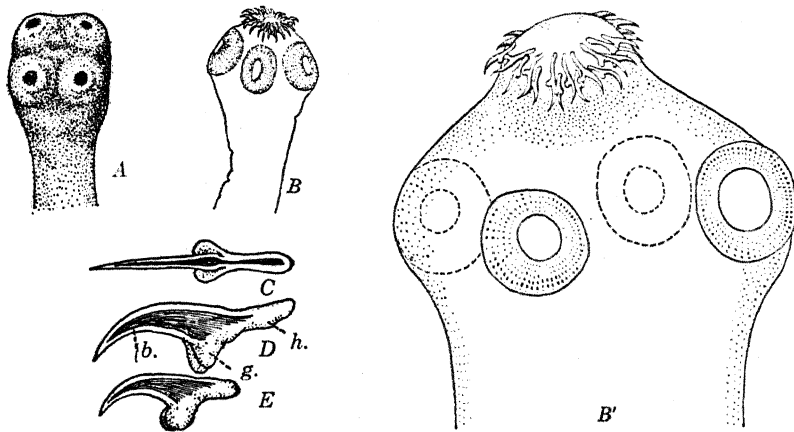


FIG. 98. A, unarmed scolex of *Taenia saginata*, $\times 10$; B, armed scolex of *T. solium*, $\times 16$; B', same, $\times 60$; C, long hook, dorsal view; D, same, lateral view; E, short hook, lateral view; b., blade; g., guard; h., handle or root; C-E, $\times 160$.

***Taenia solium* or Pork Tapeworm.** This worm is common in parts of the world where pork is eaten without thorough cooking, especially in some localities in Europe, but it is rare in the United States. In Jewish and Moslem countries, where the eating of pork is a serious religious misdemeanor, this parasite has little chance of survival and is scandalous evidence of moral turpitude when it does occur, just as is the beef tapeworm in Hindus. It is a remarkable fact that in many parts of the world, e.g., North America, India, the Philippines, human infections with adult worms are so rare that many laboratories are unable to obtain specimens, yet bladderworm infections in pigs are of fairly frequent occurrence. Even human infections with the bladderworm of this species are commoner than infections with the adult. This is one of the unsolved mysteries of parasitology.

MORPHOLOGY. The pork tapeworm (Fig. 86) usually attains a length of 6 to 10 ft., records of specimens much longer than this are probably due to confusion of parts of more than one worm; there are 800 or 900 proglottids. The scolex (Fig. 98B) is smaller than the head of a pin, about 1 mm. in diameter, and has a rostellum armed with 22 to 32 hooks, long ones ($180\ \mu$) and short ones ($130\ \mu$) alter-

nating (Fig. 98C and D). Behind the head is a thin, unsegmented neck; the younger segments are broader than long, but in the middle part of the worm they become square, and the ripe ones are about twice as long as broad, shaped somewhat like pumpkin seeds and about 12 mm. long. The sexually mature proglottids closely resemble those of *T. saginata* (Fig. 88).

Soon after sexual maturity is reached and sperms for fertilizing the eggs have been received, the uterus begins to develop its lateral branches; in this species there are only 7 to 10 main branches on each side, a fact which is of special value in distinguishing the ripe segments from those of *T. saginata*, which has about twice as many (cf. Fig. 89A, B). The fully ripe uterus usurps nearly the whole proglottid; most of the other reproductive organs degenerate.

LIFE CYCLE (Fig. 90). A man infested with a pork tapeworm expels ripe segments, singly or in short chains, almost every day. Several hundred a month are cast off, each loaded with thousands of eggs; the embryophores are nearly spherical and measure 35 to 42 μ in diameter. The shed ripe proglottids, unlike those of *Taenia saginata*, are flabby and inactive and are passed only in the feces, so pigs become infected as a result of coprophagous habits and are likely to have very heavy infections. Free eggs cannot consistently be found in the feces. The eggs probably survive for a considerable time in moist situations, as do those of *T. saginata*. The filthy way in which hogs are usually kept gives ample opportunity for their infection wherever there is human soil pollution or where privies are built in "open-back" style, or so that they leak. Young pigs are especially susceptible. The pig is not, however, the only intermediate host; the bladderworms can also develop in camels, dogs, monkeys, and man.

Upon ingestion by a suitable animal the oncospheres are liberated, bore through the intestinal wall, and make their way, via the blood or lymph channels, usually to the muscles or meat, but they may settle in almost any part of the body. They especially favor the tongue, neck, heart, elbow, and shoulder muscles, and certain muscles of the hams. Having arrived at their destination they grow into bladderworms or cysticerci, named *Cysticercus cellulosae*. The cysticerci are small, oval, whitish bodies with an opalescent transparency, 6 to 18 mm. long (Fig. 99), with a denser white spot on one side where the scolex is invaginated. Pork containing these larvae is called "measly" pork. Sometimes the cysticerci are so numerous as to occupy more than one-half the total volume of a piece of flesh, numbering several thousands to a pound.

When cysticerci in pork are eaten by man all but the scolex is digested

and it, turning right side out and anchoring itself to the wall of the small intestine, grows to maturity in about two or three months. Man is the only animal known to serve as a final host, though considerable growth takes place in dogs.

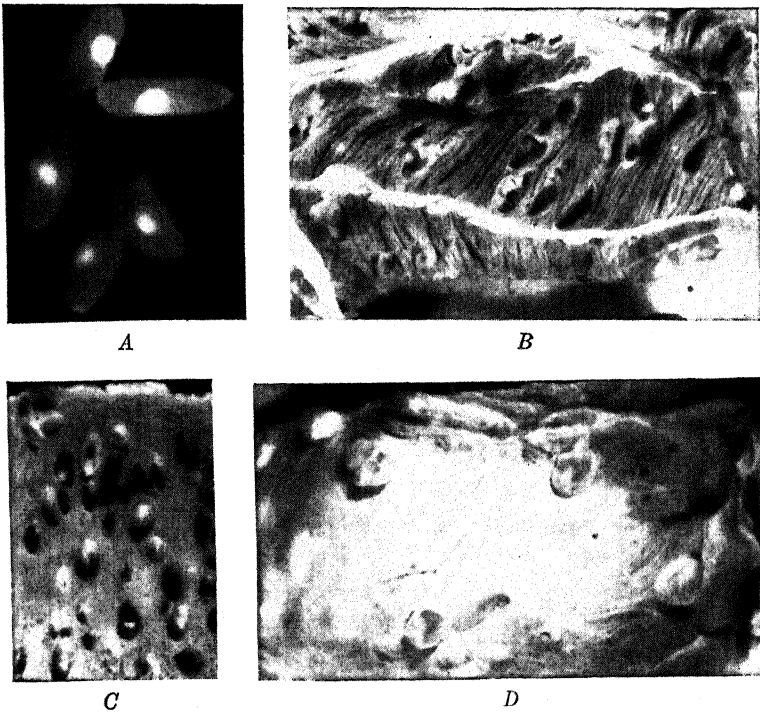


FIG. 99. *Cysticercus cellulosae*: A, freed cysticerci ($\times 1\frac{1}{2}$); B, cut pieces of "measly" pork, heavily studded with cysticerci ($\times \frac{1}{2}$); C, cut piece of pig heart, loaded with cysticerci ($\times \frac{1}{2}$); D, same, surface view (slightly reduced).

PATHOGENICITY. The adult worms in the intestine produce the same effects as *Taenia saginata* (see p. 355). This species, however, is particularly dangerous because the bladderworms as well as the adult can develop in man, causing cysticercosis. Self-infection with the eggs can result either from contaminated hands or by hatching of eggs liberated in the intestine. Since Heyneman (1955) has shown that *Hymenolepis nana* eggs thus liberated can hatch without the need of being carried back to the stomach, this may also be true of *Taenia solium* eggs. Numerous cases of cysticercosis were diagnosed in British soldiers serving in North Africa or India during World War II.

The effects depend on the location of the cysticerci in the body. A

few in the muscles or subcutaneous tissues are nothing to worry about but, chiefly as the result of mechanical pressure, they may create unpleasant disturbances when they locate in the eye, heart, spinal cord, brain, or other delicate organs.

Eye infections require surgical removal. Brain infections lead to epileptic convulsions, violent headaches, giddiness, local paralysis, vomiting, and optic and psychic disturbances, often hysteria-like in nature. Probably many such cases are never correctly diagnosed. Presence of subcutaneous cysticerci should lead to suspicion. Asenjo, in Chile, found 9 per cent of "brain tumors" to be really cysticercosis, and he has devised a method by which even one cysticercus can be identified by ventriculographic x-ray. If the cysticerci are numerous, surgical removal may be impractical, but no other treatment is known.

Prevention, and treatment for expulsion of adult worms in the intestine are discussed on pp. 340-341.

***Taenia saginata* or Beef Tapeworm.** This is the commonest large tapeworm of man and is cosmopolitan in distribution. In some localities, e.g., parts of Africa, Tibet, and Syria, where meat is broiled in large chunks over open fires, searing the surface but making the cysticerci in the interior only comfortably warm, it infects 25 to 75 per cent of the people old enough to eat meat. In the Hindu sections of India *T. saginata* is religiously ostracized, since only the lowest outcast will eat the meat of the sacred cow or even of water buffaloes.

MORPHOLOGY. The beef tapeworm ordinarily reaches a length of 15 to 20 ft., but specimens up to 35 to 50 ft. have been recorded; the proglottids of an average worm number 1000 or more. The scolex (Fig. 98A) is 1.5 to 2 mm. in diameter and is without hooks. Both mature and ripe segments (Figs. 88 and 89A) are larger than those of *T. solium*. The detached terminal segments are about 20 mm. long and 6 mm. wide when relaxed. When freshly passed, usually singly, they are firm and very active, and crawl away like caterpillars; often they creep out of the anus and deposit eggs from the ruptured ends of the uterus on the perianal skin (see p. 339). Several times active specimens from the surface of a fresh stool have been sent to the writer as some new kind of fluke!

LIFE CYCLE. The life cycle is similar to that of *Taenia solium* except that usually the intermediate hosts are cattle or allied animals. However, giraffes, llamas, and pronghorn antelopes are occasionally infected with cysticerci, and lambs and kids have been experimentally infected; two valid human cases have been recorded. In the tropics cattle and buffaloes, habitually coprophagous, often have their flesh thoroughly riddled by the cysticerci. In India cattle, like pigs, frequently follow

human beings to the defecation sites in anticipation of a fecal meal. Under favorable conditions the eggs remain viable in pastures for 6 months. The cysticerci (named *Cysticercus bovis*) in measly beef are 7.5 to 10 mm. wide by 4 to 6 mm. long. They are most frequently present in the muscles of mastication and in the heart; these are the portions of the carcass usually examined in meat inspections. They are, however, inconspicuous and can easily be overlooked in raw or rare beef.

PATHOGENICITY. The damage done by adult taenias to their hosts is often either under- or overrated. There are some who believe that the presence of a tapeworm is more or less of a joke, and as such to be got out of the system but not to be taken seriously, whereas others become unnecessarily disturbed over them. They may cause mechanical injury by obstructing the intestinal canal and by injuring the mucous membranes where they adhere, and they may absorb enough nourishment to produce the proverbially ravenous "tapeworm appetite," although much more frequently they cause *loss* of appetite.

Swartzwelder in 1939, in a series of sixty cases in New Orleans, found abdominal pain, excessive appetite, weakness, and loss of weight to be the commonest symptoms. Other symptoms are nausea, difficult breathing, digestive disturbances, dizziness, insomnia, restlessness, false sensations, and occasionally convulsions and epileptic fits. Many of these symptoms might well be due to an induced vitamin deficiency in hosts on a marginal or suboptimal supply, which is deplorably common even in the relatively well-fed United States. The writer (1943) showed that tapeworms thrive even when there are no vitamins in the diet of the host, and that some and probably all that are needed are acquired directly from the host. Anemia and eosinophilia are rare. The writer knew of a case in which tuberculosis was suspected; the patient was weak, easily exhausted, and emaciated, with sunken cheeks and staring eyes. A fortnight after two large *Taenia* were expelled he was like a new man. In contrast, a colleague harbored a *Taenia* for years; in spite of a number of unsuccessful efforts to part company with it, "Horace," as he familiarly called his guest, stayed with him, yet there were never any symptoms other than segments in the stools, and the host continued in ruddy and robust health. The latter case is, perhaps, much more common than the former. For diagnosis see p. 339; for treatment and prevention, pp. 340-341.

Other Species of *Taenia* and *Multiceps*. The genus *Taenia* and the genus *Multiceps*, distinguishable only by the multiple heads produced in the larvae of *Multiceps*, include many species parasitic as adults in dogs and cats and as larvae in herbivores. Some of the commonest

ones in dogs are *T. pisiformis* (= *serrata*), the larvae of which develop in the liver and mesenteries of rabbits; *T. ovis*, developing in the connective tissue in muscles of sheep; *T. hydatigena*, developing in the liver of sheep; *M. multiceps* (Fig. 100), developing as a coenurus in the brain of ruminants and causing gid; and *M. serialis*, developing in subcutaneous connective tissue of rabbits. *T. pisiformis* and *T. hydatigena* occur also in cats, but the commonest form in these animals is *T. taeniaeformis*, which develops in the livers of rats and mice. One human

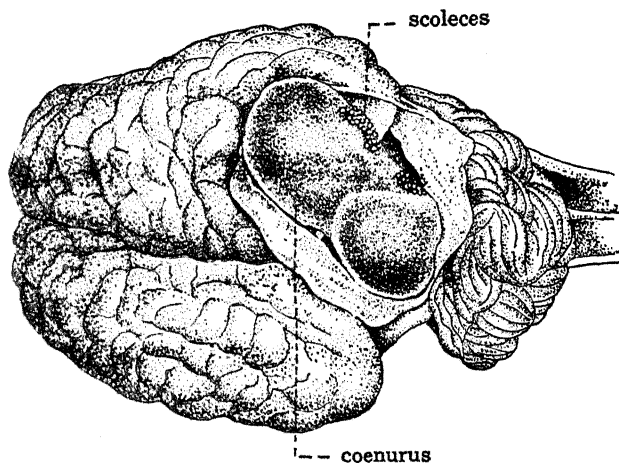


FIG. 100. Brain of giddy sheep with coenurus of *Multiceps multiceps*, showing masses of scoleces. (After Neumann, from Hall.)

case is recorded. The bladderworm of this species, *Cysticercus fasciolaris*, contains a considerable chain of undeveloped segments and is sometimes called a strobilocercus. All these worms resemble *T. saginata* except in minor details; the scoleces differ in the number and size of the hooks.

About a dozen cases of coenurus infection in man have been recorded: several brain infestations with *M. multiceps* (*Coenurus cerebralis*), one of which caused epileptic symptoms; a number of muscular or subcutaneous infections, some identified as *M. serialis* and at least one of the others as *M. glomeratus*, previously described from a gerbil. Crusz in 1948 suggested that these are possibly all one species. The species of *Multiceps* are distinguished mainly by the number, size, and shape of the rostellar hooks.

A few rare species of adult *Taenia* have been found in man. Four cases of "*T. confusa*" have been reported in the United States and three

from eastern Africa, but Anderson (1934) believes this form to be only a variant of *T. saginata*. Probably *T. bremneri*, described from a Nigerian, is the same thing. Another species, of which two specimens were obtained from an East African, is *T. africana*. It has segments broader than long, and unarmed scolex, and a uterus with unbranched arms.

1980 ✓ 8. how it differs from alveolar & coelocous ones?
***Echinococcus* and Hydatid Cysts.** The genus *Echinococcus* contains several species of very minute tapeworms which live as adults in the intestines of dogs and dog-like animals, except one species found in pumas and jaguars in South America. The larvae of these tiny worms, in contrast, develop into huge hydatid cysts in many herbivorous animals. Only one species, *E. granulosus*, has thus far been recognized as producing hydatid cysts in man and domestic animals, but it is possible that any of the species may do so, and there is reason to believe that the alveolar type of hydatid cysts (see below), known only from parts of central Europe, may be caused by a distinct species.

E. granulosus has both a sylvatic and a pastoral epidemiology. The infestation is best known, naturally, in the areas where it is passed back and forth between dogs and sheep or cattle, and more or less frequently to man. It is especially prevalent in such sheep and cattle-raising areas as North and South Africa, the Middle East, Australia, New Zealand, southern South America, and until recently Iceland. Today the infection is becoming rare in Iceland, except in elderly people. In many of the areas mentioned above, one-fourth of the dogs and half of the animals are infected; in the Middle East hydatids occur in about 20 per cent of sheep, 40 per cent of cattle, and 100 per cent of camels. In northern Scandinavia there is a dog-reindeer cycle.

The sylvatic form of the disease occurs particularly in circumpolar areas, where wolves and moose or deer are principally involved, and in Australia, where the parasite oscillates between dingoes and wallabies. A particularly interesting situation exists in Siberia and St. Lawrence Island (Alaska), where the infection passes between foxes and rodents (*Microtus* and *Clethrionomys*). Rausch (1954) found a different species, *E. sibiricensis*, involved, characterized by infecting rodents in the larval stage and by producing alveolar cysts through exogenous budding. Rausch suggests that this species may be responsible for the human alveolar hydatids in Europe and Siberia (see pp. 359-360).

MORPHOLOGY. The adult (Fig. 101) is structurally much like a *Taenia*, but is very unlike it in size, and the ripe uterus has a broader central stem with only lobe-like out-pocketings, which are often indistinct. The worm is only 2 to 8 mm. long, and consists of a scolex and neck followed by only three or four successively larger segments,

one immature, one or two mature, and usually one ripe or nearly ripe. The head has a protrusible rostellum armed with a double row of 28 to 50 hooks, usually 30 to 36. The worms occur by hundreds or even thousands in the intestines of dogs but are usually overlooked on account of their minute size. Each ripe segment contains 500 to 800 eggs. In spite of the small size of the adult worms, they require 4 to 6 weeks to mature in a dog.

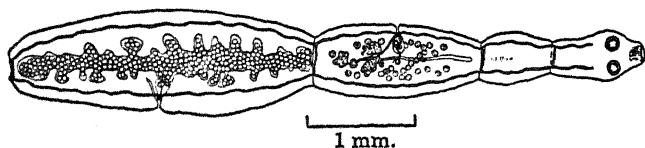


FIG. 101. *Echinococcus granulosus*. (After Mönnig, *Veterinary Helminthology and Entomology*, 1949.)

✓ **DEVELOPMENT OF HYDATIDS.** The eggs, about 30 by 38 μ , are indistinguishable from those of dog taenias. From the feces of dogs, wolves, or foxes they gain access to their intermediate hosts with contaminated forage or water. In addition to the animals noted above, pigs, horses, rabbits, and many other herbivores are susceptible. Human infection usually results from too intimate association with dogs; children are especially liable to infection by allowing dogs to "kiss" them or lick their faces with a tongue which, in view of the unclean habits of dogs, is an efficient means of transfer of tapeworm eggs. Eggs got on the hands from an infected dog's fur is also a good means of infection. Rausch and Schiller suspected that on St. Lawrence Island, man was projected into the fox-rodent picture by the prevalent habit of eating raw, unwashed greens which might have been contaminated by the abundant foxes.

In moose, deer, and caribou the hydatids develop almost exclusively in the lungs, but in domestic animals the liver and other organs are more frequently sites, and in man about 60 to 75 per cent of the cysts develop in the liver, only about 20 per cent in the lungs. Smaller numbers reach the kidneys, spleen, muscles, bone, heart, brain, and other organs.

Development of the cysts is slow. The young larva changes into a hollow bladder, around which the host adds an enveloping, fibrous cyst wall. At the end of a month these cysts measure only about 1 mm. in diameter; in 5 months they are about 10 mm. in diameter and the inner surface is beginning to produce hollow brood capsules. These ultimately remain attached only by slender stalks and often fall free

into the fluid-filled cavity of the mother cyst. As the cyst grows larger more brood capsules form, and the older brood capsules begin to differentiate, on their inner walls, a number of scoleces, usually 3 or 4 to 30 (Figs. 102, 103). Sometimes the mother cyst, as the result of pressure,

develops hernia-like buds which may detach themselves and continue their development independently as daughter cysts. The fluid of the cysts is nearly colorless; in older cysts there is a granular deposit consisting of liberated brood capsules and free scoleces, called "hydatid sand." A cyst of 2 quarts capacity may produce more than 2 million scoleces.

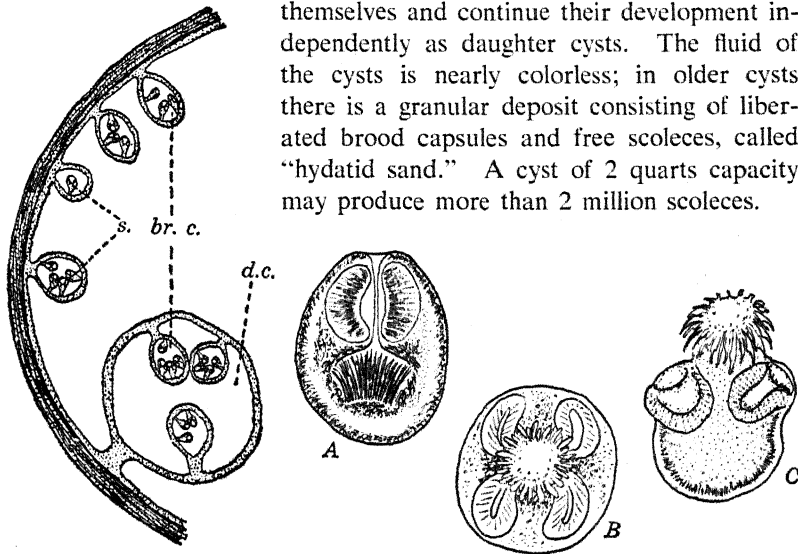


FIG. 102. Left, diagram of small hydatid cyst of *Echinococcus*, showing daughter cyst (d.c.), brood capsules (br.c.), and scoleces (s.). Stippled inner wall of cyst is part of parasite; outer fibrous wall is capsule laid down by host. Right, scoleces from cyst; A, invaginated; B, head-on view; C, evaginated.

Eventually the cysts may reach the size of an orange or larger. After 10 to 20 years they may reach enormous size and contain 10 to 15 quarts of liquid, or occasionally even more. When growth is unobstructed the cysts are more or less spherical, but they are often deformed by pressure. When developing in bones they fill the marrow cavities and may cause bone erosion. In 25 per cent of human cases more than one cyst is present, either due to original multiple infection or to development of detached daughter cysts. Not infrequently cysts fail in their primary purpose of producing scoleces and remain "sterile." Possibly this is connected with natural or acquired immunity in the hosts.

✓ **MULTILOCLAR CYSTS.** Sometimes, instead of forming a single large vesicle, the larva forms a sponge-like, constantly growing mass of small separate vesicles embedded in a fibrous tissue. It is not delimited by a capsule formed by the host, and the vesicles contain a gelatinous sub-

stance instead of fluid. Roots grow out into neighboring tissues. The central portions degenerate and die while growth continues on the outside, as in a true malignant tumor. Often portions of the growth become separated and continue to grow like the parent; such detached portions may be carried to distant parts of the body. This type of

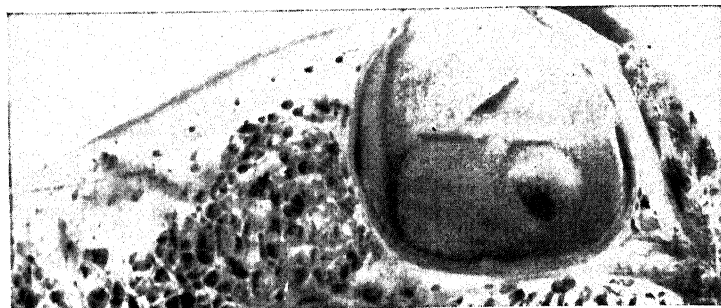


FIG. 103. Cut hydatid cyst showing numerous scoleces like velvet on inner surface.

hydatid known as a multilocular or alveolar cyst develops principally in the liver. It occurs in central Europe and Siberia, and was believed by Henschen and Bircher (1945) to be caused by a distinct species. Rausch thinks these alveolar cysts may be caused by *E. sibiricensis* (see p. 357).

✓ **PATHOLOGY.** In their natural wild hosts hydatid cysts are practically harmless, and this is frequently true in domestic animals and man also. Usually they do serious harm only when they grow to outrageous size in the liver and press on other organs; or liberate their fluid by leaking or rupturing, thus precipitating severe allergic symptoms; or develop in such organs as the kidneys, spleen, brain, or eye. When cysts are ruptured, scattered scoleces and brood capsules develop into metastatic cysts; this is especially dangerous if rupture into a blood vessel occurs.

✓ **DIAGNOSIS.** Probably most hydatid cysts in either man or animals are detected only at autopsy. In suspected cases precipitation or complement-fixation tests are possible, using hydatid fluid or an extract of adult *Taenia* as antigen, but a skin test with these antigens, called the "Casoni reaction," is better and easier. Diagnosis by x-ray is often possible, especially for pulmonary cysts, but in the liver the cysts are detectable only when calcified (see Miller, 1953).

✓ **TREATMENT AND PREVENTION.** Treatment is purely surgical, but this parasite grows fast to the fibrous walls formed by the host and does not "shell out." It is dangerous to withdraw fluid directly, and it is customary to withdraw part of the fluid with a trocar and replace it at

once, unless in the lung, with a formalin solution to kill the scoleces, brood capsules, etc. Subsequently the fluid can be drained out. Multilocular cysts can seldom be operated on successfully, and generally lead to death in a few years.

Prevention consists in avoiding too much intimacy with dogs; carefully washing hands after handling them, and also washing dishes from which they have eaten; and avoiding food or water which may have been contaminated by them. Care should also be taken that dogs are not fed, or do not get access to, the entrails or waste parts of slaughtered or dead animals from which they can become infected.

The practical elimination of the disease in Iceland was accomplished by licensing and annual treatment of dogs, and enforcing the burial or burning of infected material. Arecolin hydrobromide, one-sixteenth grain per 10 lb. wt., eliminates 95 per cent of *Echinococcus* from dogs; 3 doses usually eliminate all, and most *Dipylidium* and *Taenia* as well.

HYMENOLEPIDIDAE

This family contains a large number of species of tapeworms parasitic in birds and mammals, particularly in the former. Their characteristics are summarized on p. 350. Three species have been found in man. One, *Hymenolepis nana*, is a very common parasite of man and of rats and mice; another, *H. diminuta*, is abundant in rats and mice but relatively rare in man, though by no means a curiosity; the third, *H. lanceolata*, is a parasite of ducks and geese and has been recorded from man only once.

Hymenolepis nana. The dwarf tapeworm, *H. nana*, is the smallest adult tapeworm found in man, but it makes up for its diminutive size by the large numbers which are often present. It has a world-wide distribution, but it is far commoner in some localities than in others. It is the commonest tapeworm in southern United States, where about 1 to 2 per cent of the population, especially children, are infected. Sunkes and Sellers in 1937 collected data on 927,625 fecal examinations in the southern states and got records of 8085 tapeworm infections; all but 100 of these (98.6 per cent) were *H. nana*. In some parts of India as high as 18 to 28 per cent of the population were found by the writer to be infected. In 500 Egyptian villagers examined by the writer, 36 *H. nana* infections were found (7 per cent), but all but 2 of these were in children below the age of puberty.

The adult worm ranges from 7 to over 100 mm. in length. In general the length of the worms is inversely proportional to the number present; in heavy infections it is commonly 20 to 30 mm., with a maximum breadth of only 500 to 600 μ ; it is seldom found after treatment,

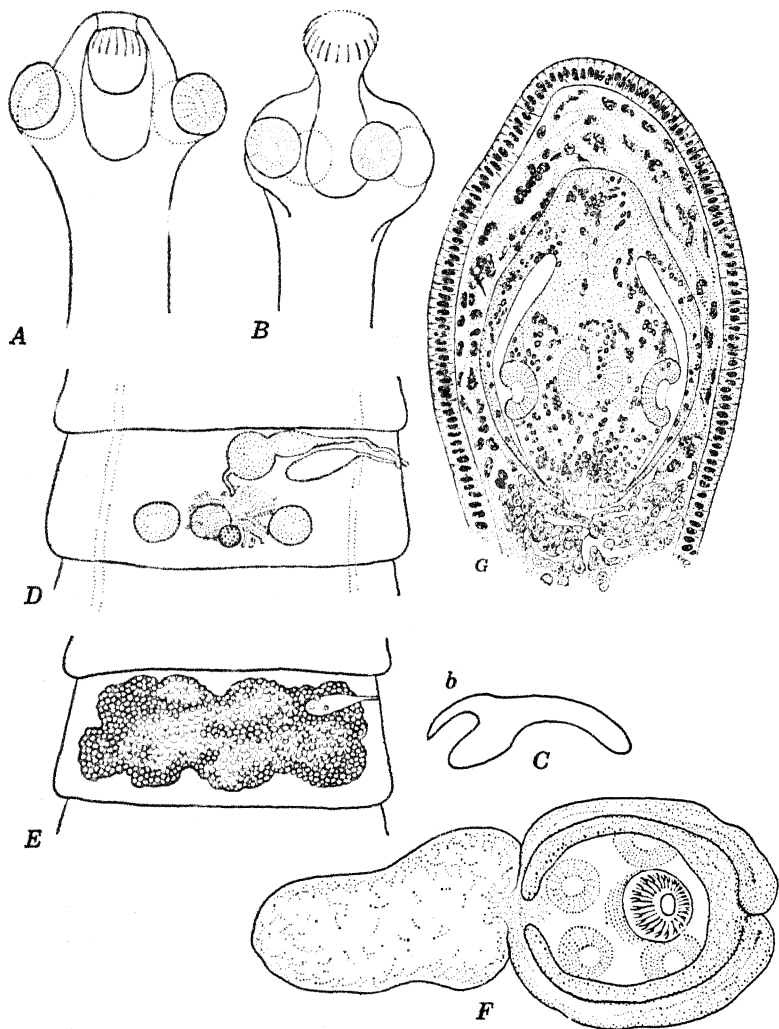


FIG. 104. *Hymenolepis nana*: A, scolex with rostellum retracted; B, same, rostellum exerted; C, rostellar hook, blade (*b*) up; D, mature segment; E, ripe segment; F, cysticercoid from body cavity of *Tribolium*; G, cysticercoid in villus of mouse intestine. (G, adapted from drawing by W. S. Bailey.)

even when diligently sought. The scolex (Fig. 104A and B) has a well-developed retractile rostellum with a crown of 20 to 30 hooks. All the proglottids are considerably broader than long. The arrangement of the organs in mature proglottids can be seen in Fig. 104E. The uterus develops as a sac which practically fills the segment between

the excretory vessels. The uterine walls and partitions between segments may break down to allow passage of eggs from segment to segment, and out from the broken posterior end of the worm.

The eggs have a very characteristic appearance (Fig. 57O). The outer shell is oval, thin, and practically colorless; it commonly measures about 40 by 50 μ . The embryophore is lemon shaped, 16 to 20 μ long, with a little knob at either end from which arise a number of long, delicate, wavy filaments which lie in the space between the embryophore and the outer shell. All six embryonic hooks lie approximately parallel in healthy oncospheres.

LIFE CYCLE. *Hymenolepis nana* differs from almost all other tapeworms in being able to complete its entire life cycle in a single host. In this it is radically progressive, having broken away from the age-old tapeworm custom of utilizing intermediate hosts. It can, however, still revert to the habits of its ancestors and develop in fleas or grain beetles. When the eggs are ingested by man, rats, or mice, the oncospheres begin to claw actively inside their shells, and escape in the lumen of the intestine. They burrow into the interior of the villi and there develop into tailless cysticercoids in about 4 days (Fig. 104G). On reaching maturity these escape into the lumen of the intestine, the scoleces attach themselves, and the worms grow to maturity in about 15 to 20 days. In grain beetles, however, development of the tailed cysticercoids (Fig. 104F) takes 12 to 14 days.

In egg infections, since the worm is parenterally located during development of the cysticercoid, immunity develops, but not after cysticercoid infections. Heyneman (1955), however, found that the immunity developed by an egg infection also affects worms acquired from subsequent cysticercoid infections, showing that tapeworms in the lumen of the intestine, although incapable of getting antigens into the body to stimulate antibody production, are susceptible to the antibodies if they are produced. Heyneman also showed that after non-immunizing cysticercoid infections, eggs produced by the worms hatch in the intestine and produce a massive secondary infection. Such a mechanism may account for the frequent heavy infections in man. In the large human intestine even a small egg infection acquired from a mouse dropping might permit autoreinfection to occur, producing hundreds or even thousands of worms to develop.

RELATION OF HUMAN AND RODENT STRAINS. The identity or otherwise of *H. nana* of man and *H. nana fraterna* of mice and rats has been much disputed. The human infection is relatively rare in some localities, especially northern Europe and Canada, where the rodent infections are common, and although eggs of human worms will develop in

rodents, and vice versa, this does not occur as readily as when the eggs are ingested by the same hosts as those from which the eggs were derived. Shorb (1933) found similar differences between strains from rats and mice.

In India, however, the writer (1927) found an inverse correlation between the incidence of *H. nana* infections and that of *Ascaris* and *Trichuris*, which depend on human fecal contamination for transmission, but a direct correlation with prevalence of household rodents and conditions favoring their access to food, and with such rodent-borne infections as plague and *H. diminuta*. The fact that in our southern states *H. nana* infections are about equally common in cities with sewerage systems and in rural areas is also more suggestive of dissemination by rats and mice than by human contamination. Prevention, therefore, would seem to depend primarily on preventing access of mice or rats to food that is to be eaten without further cooking.

H. nana causes rather severe toxic symptoms, especially in children, including abdominal pain, diarrhea, convulsions, epilepsy, insomnia, and the like. Diagnosis is easily made by finding the eggs in the feces; like nematode eggs, they float in strong salt solutions. Treatment is considered on p. 340.

Other Species of *Hymenolepis*. *H. diminuta*, very common in rats and mice in all parts of the world, is much less common in man. It is a much larger worm than *H. nana*, reaching a length of 1 to 3 ft., with a maximum diameter of 3.5 to 4 mm. The head (Fig. 105B), unlike that of nearly all other species of *Hymenolepis*, is unarmed, and the segments (Fig. 105A) are much broader than long. The structure of mature and ripe segments is much like that of *H. nana*. The eggs (Fig. 57N) are larger (60 to 80 μ in diameter), yellow or yellow-brown, and usually spherical. The oncosphere lacks the knob-like thickenings at the poles, or at best they are rudimentary, and there are no filaments.

Like most kinds of *Hymenolepis* this worm requires an intermediate host for the development of its cysticercoids (Fig. 105C). It is satisfied with any one of many grain-infesting insects, including larvae and adults of meal moths (*Pyralis farinalis*), nymphs and adults of earwigs (*Anisolabis annulipes*), adults of various grain beetles such as *Tenebrio* and *Tribolium*, dung beetles, the larvae of fleas, and even myriapods. Human infection results from eating such foods as dried fruits and precooked breakfast cereals in which the grain insects, infected from rat or mouse droppings, are present. Until about 1925 this infection was considered sufficiently rare in man so that every instance was published as an incident worthy of note, but the writer found 23 cases in about 10,000 fecal examinations in India and found

no less than 3 in 50 examinations in one locality where the food habits and rat population were particularly favorable. He also found 9 cases (nearly 2 per cent) in examinations of 500 Egyptian villagers. As is

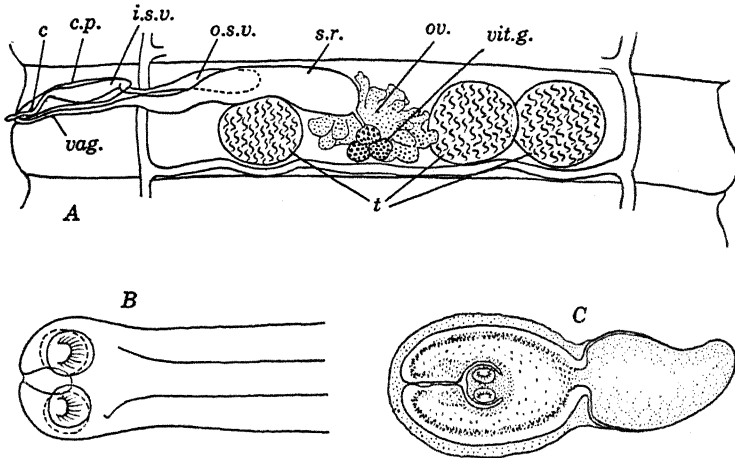


FIG. 105. *Hymenolepis diminuta*: A, mature segment; B, scolex; C, cysticercoid from *Tenebrio* beetle; c., cirrus; c.p., cirrus pouch; i.s.v., inner seminal vesicle; o.s.v., outer seminal vesicle; ov., ovary; vag., vagina; vit.g., vitelline gland.

usually true with human tapeworms which belong in another host, this worm is very easily expelled by anthelmintic treatment and is sometimes expelled spontaneously or after a cathartic.

DIPYLIDIINAE

***Dipylidium caninum*.** Although many species of *Dipylidium* have been described, Venard (1938) thinks nearly all of them are really one species, *D. caninum*, an extremely common parasite of flea-infested dogs and cats all over the world. Over 100 human cases, nearly all in children, have been reported, but the actual number of cases is undoubtedly much greater. One doctor from one Texas city has sent the writer three specimens from children for identification. *D. caninum* is a delicately built tapeworm, commonly reaching a length of about a foot. The peculiar characteristics of the scolex and proglottids are mentioned on p. 350 and illustrated in Fig. 106. The uterus first develops as a honeycomb-like network, but later breaks up into egg balls, each containing 5 to 20 eggs, which remain intact even when the segments disintegrate. The ripe proglottids are the size and shape of elongated pumpkin seeds and are often seen squirming actively in the freshly passed feces of infected animals.

The intermediate hosts are fleas (*Ctenocephalides* and *Pulex*) and dog lice (*Trichodectes canis*). Joyeux (1920) observed that the eggs could not be ingested by adult fleas but are devoured by the larvae. The embryos hatch in the intestine and bore through into the body

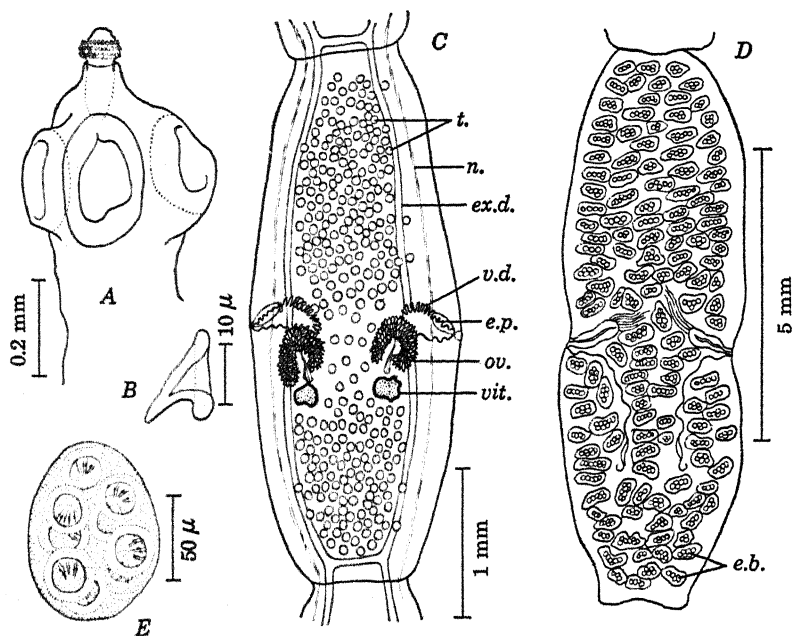


FIG. 106. *Dipylidium caninum*: A, scolex, showing rostellum with 4 rows of hooks; B, rose-thorn rostellar hook; C, mature proglottid; D, ripe proglottid filled with egg balls; E, single egg ball. Abbreviations: c.p., cirrus pouch; e.b., egg balls; ex.d., excretory duct; n., lateral nerve; ov., ovary; t., testes; v.d., vas deferens; vit., vitellaria. (D, adapted from Hall, *Proc. U.S. Natl. Mus.*, 55, 1919. Others from Witenberg, *Z. Parasitenk.*, 1932.)

cavity, where they remain very little changed until the flea has transformed into an adult, whereupon it develops into a cysticercoid which infects the final host when the flea is nipped. Children are probably infected by having their faces licked by a dog just after the dog has nipped a flea.

ANOPLOCEPHALIDAE

The Anoplocephalidae, the principal characters of which are mentioned on p. 350, are very common parasites of herbivorous animals, including cattle, sheep, goats, horses, camels, rabbits, rodents, and also apes and pigeons. They are often present in very young animals, and the incidence of infection may be very high.

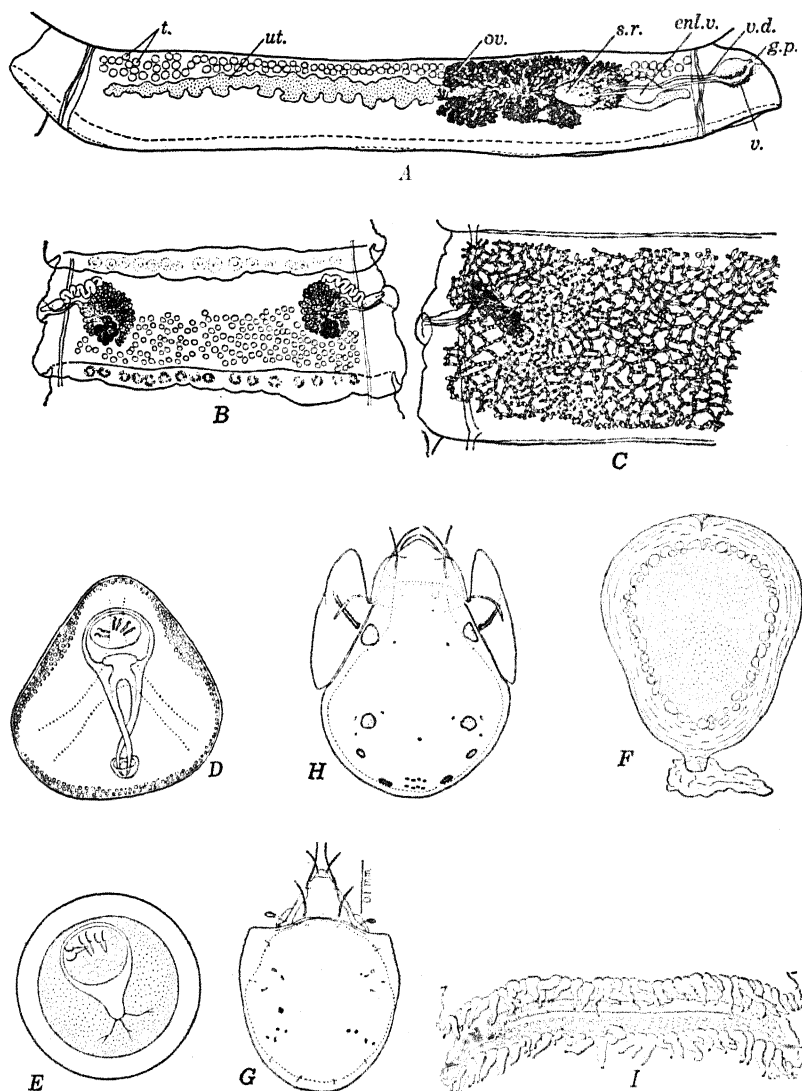


FIG. 107. Anoplocephalids and vectors. A, *Bertiella studeri*, mature segment (from Chandler, *Parasitology*, 17, 1925). B, *Moniezia expansa*, mature segment, and C, same, left half of ripe segment (after Fuhrmann from Wardle and McLeod, *The Zoology of Tapeworms*, 1952). D, egg of *Moniezia* (adapted from Mönnig, *Veterinary Helminthology and Entomology*, 1949). E, egg, and F, cysticercoid of *Bertiella studeri* (after Stunkard, *Am. J. Trop. Med.*, 20, 1940). G, *Protoschelobates seghettii*, and H, *Galumna virginensis*, intermediate hosts of *Moniezia expansa* (after Kates and Runkel, *Proc. Helm. Soc. Wash.*, 15, 1948). I, *Thysanosoma actinioides*, fringed tapeworm (after Fuhrmann in Kükenthal, *Handbuch der Zoologie, Vermes Amera*).

The life cycle of these worms was one of the outstanding mysteries of parasitology until Stunkard (1937) succeeded in developing the cysticercoids of *Moniezia* of cattle and sheep in oribatid mites (see p. 543). The mites (Fig. 107G, H), living about the roots of grass, are seldom seen but may be very abundant and are undoubtedly often eaten by grazing animals. In a pasture at Beltsville, Md., there were estimated to be 6,000,000 oribatid mites (*Galumna virginiensis*) per acre, nearly 4 per cent of them harboring 1 to 13 *Moniezia* cysticercoids—400,000 potential tapeworms per acre!

Since Stunkard's work a dozen other anoplocephalid tapeworms have been found to develop in oribatid mites, and probably all members of the family do so, now that the former subfamily Linstowiinae has been eliminated and elevated to the rank of a separate family. The development of cysticercoids of typical anoplocephalids in oribatid mites is very slow, taking 5 to 15 weeks.

Many animals harbor anoplocephalid infections. *Moniezia* (Fig. 107B-D) are large worms of cattle, sheep, and goats, reaching 10 ft. or more in length, with double sets of reproductive organs in the proglottids. Sheep and goats in western United States commonly harbor the fringed tapeworm, *Thysanosoma actinioides* (Fig. 107I) characterized by fringes on the posterior borders of the segments. Horses harbor a number of species, but the most important are two rather short, thick worms of the genus *Anoplocephala*: *A. magna*, about 10 in. long, in the small intestine, and *A. perfoliata*, only 1 to 2 in. long, in the cecum. Rabbits are commonly afflicted by members of the genus *Cittotaenia*. Young animals are said to suffer digestive disturbances and retarded growth from anoplocephalid infections if their nutrition is poor, as might be expected, but Kates and Goldberg (1951) found no evidence of injury in well-fed lambs.

Human infection with members of this family is limited to *Bertiella studeri* (Fig. 107A, E, F) normally parasitic in apes and monkeys. This worm has been reported from man only 11 times, mostly in children. It is a thick, opaque worm 25 to 30 cm. long and 10 to 15 mm. broad. The arrangement of organs is shown in Fig. 107. The ripe proglottids are very broad, but less than 1 mm. in length; they are shed in blocks of 20 or more. Most of the human cases have occurred around the Indian Ocean, but the infection appears also to have been established in the West Indies—an example of the danger of introducing foreign species of worms with captive animals. Stunkard (1940) developed minute cysticercoids (0.1 to 0.15 mm. in diameter) in oribatid mites but was unsuccessful in infecting man or monkeys with them.

LINSTOWIIDAE

This family, which includes the large genus *Oëchoristica*, with species in reptiles, birds, and mammals, contains tapeworms which resemble the Davaineidae closely except in having unarmed scoleces. The only life cycles known involve beetles. One member of this family, *Inermicapsifer arvicanthidis* (= *I. cubensis*) (Fig. 108) parasitizes man. This worm was first found in children in Cuba by Kourí, and was named

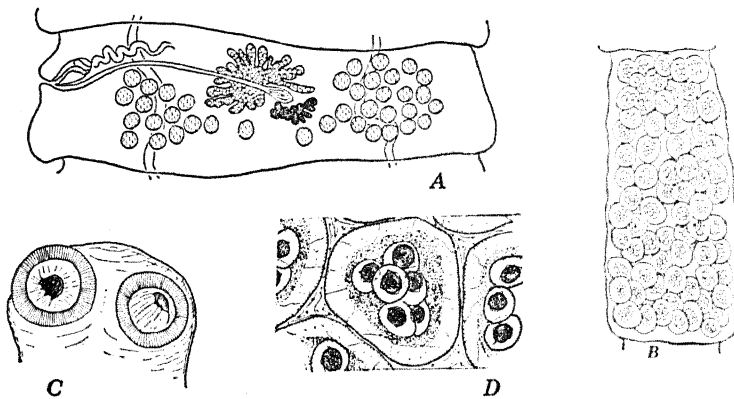


FIG. 108. *Inermicapsifer arvicanthidis* (= *cubensis*). A, mature proglottid; B, ripe proglottid; C, scolex; D, egg capsules. (From Baer, Kourí and Sotolongo, *Acta Tropica*, 1949.)

I. cubensis. Over 100 human infections have been reported in western Cuba. Later Fain (1950) showed that this worm is the same as *I. arvicanthidis*, common in small rodents in Africa, and found twice in human infants in central Africa. The worms are 2 to 3 ft long, the ripe segments 3 to 4 mm. long and 1 to 2 mm. wide. It seems highly probable that the worm was introduced into Cuba in rodents from Africa, for all the other dozen or so species of *Inermicapsifer* are parasites of hyraxes or rodents in Africa.

DAVAINEIDAE

The majority of the tapeworms in this family are parasitic in birds, and several are common and injurious parasites of poultry. The general characteristics are given on p. 350. The cysticercoids of the chicken parasites develop in various intermediate hosts: the minute but injurious *Davainea proglottina* in slugs; *Raillietina tetragona* in maggots of the housefly; *R. echinobothrida*, another particularly pathogenic species, in an ant; and *R. cesticillus* in various beetles. Phenylmercuric com-

pounds in a dose of 50 mg. are effective against *R. cesticillus* but not against the others.

A number of cases of human infection with worms of the genus *Raillietina* have been recorded from various parts of the world—

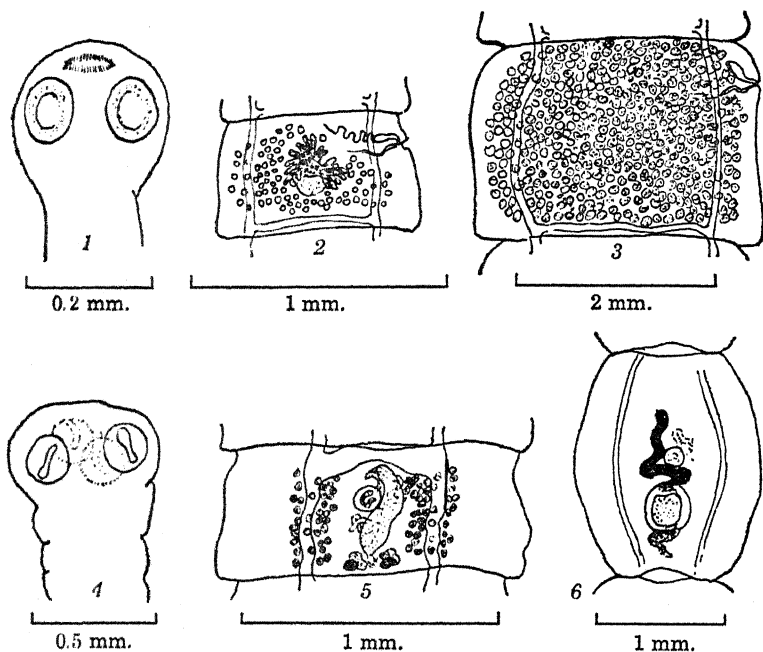


FIG. 109. Upper row, *Raillietina*, from man in Ecuador (*R. demerariensis*?): 1, scolex, with double crown of about 150 small hooks, and minute spines on suckers; 2, mature proglottid; 3, ripe proglottid, with about 200 to 300 egg capsules, each with about 7 to 10 eggs. (After drawings and description by Dollfus, *Ann. Parasitol. hum. et comp.*, 17, 1939-1940.) Lower row, *Mesocestoides variabilis*, from child in Texas; 4, scolex, showing slit-like openings of suckers; 5, mature proglottid, showing yolk glands and ovaries posteriorly; cirrus pouch near center; developing uterus; convoluted vagina; and testes on both sides of excretory canals; 6, ripe proglottid, showing egg ball, remnants of uterus, and cirrus pouch. (After Chandler, *Am. J. Trop. Med.*, 22, 1942.)

in seaports around the Indian Ocean and South China Sea from Madagascar to Japan, in Cuba, and in Guiana and Ecuador in South America. The human cases undoubtedly represent accidental infections with species parasitizing local wild mammals.

For many years all the Old World human cases were referred to the species *R. madagascariensis*, but it now seems probable that several species may be involved, all of them, as far as known, primarily parasites of rats. The South American forms, reported from Guiana and

Ecuador, have also been thought to represent several species, but Joyeux and Baer (1949) believe they may all be one, *R. demerariensis* (Fig. 109, 1-3), normally parasitic in howler monkeys (*Alouatta*). These species of *Raillietina* are slender worms reaching a length of 1 to 3 ft., with a maximum width of 3 to 8 mm. All the genital pores are on one side. The scolex has a double crown of small hooks (Fig. 109, 1), and the suckers are armed with a number of rows of minute spines. The ripe proglottids are usually squarish or elongate and contain about 100 to 400 egg capsules, each with several elongated eggs.

There is no question but that these worms utilize some arthropod as an intermediate host.

MESOCESTOIDIDAE

The genus *Mesocestoides* has the peculiar characters listed for Mesocestoididae on p. 350, including a posterior paruterine organ or egg ball (Fig. 109, 4-6). The number of species has been much disputed, since the worms show considerable variation and there are no good differential characters. The entire life cycle is unknown. *Sparganum*-like larvae called tetrathyridea occur free or encysted in reptiles, birds, and mammals, but these are probably second larval stages. The first human infection with a *Mesocestoides* was reported by the writer (Chandler, 1942) from a child in east Texas. The worms, estimated up to 40 cm. long and about 1.6 mm. wide, are probably *M. variabilis*, previously known from foxes, skunks, raccoons, and dogs in the United States. Subsequently another case was found in a Greenlander in Denmark.

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Acanthocephala (Spiny-Headed Worms)

As noted on p. 242, the Acanthocephala have usually in the past been attached as a rider to the Nemathelminthes for want of a better place to put them, but as Van Cleave (1941) pointed out, they have much more affinity to the Platyhelminthes, particularly the Cestoidea, both in structural characteristics and in life cycle. Van Cleave (1948) raised them to the rank of a phylum. They are all intestinal parasites, found in all classes of vertebrates, though especially common in fishes and birds. They are remarkably uniform in general anatomy, life history, and habits.

Morphology. Like tapeworms, Acanthocephala are devoid of an alimentary canal throughout their lives. The body is divided into a posterior trunk and an anterior presoma, consisting of a spiny proboscis and unspined neck. In some the neck is a short transitional area; in others it may be long and conspicuous. The trunk and presoma are demarcated by an infolding of the cuticula and the derivation from the hypodermis of two elongate structures of unknown function called lemnisci (Fig. 110A) which lie in the body cavity. The proboscis, and often the neck also, is in most species retractile into a proboscis sac or receptacle by being turned inside out, and the whole presoma is also retractile, without inversion, into the fore part of the trunk by means of special retractor muscles inserted on the trunk wall (Fig. 110A, *r.m.*). The armature of the proboscis varies from a few to a great many hooks, which are usually in radial or spiral rows; in long proboscides they appear to be in longitudinal rows with quincunxial arrangement (Fig. 112).

The body is covered with a cuticle under which is a syncytial hypodermis or subcuticula. In more primitive forms this has a small number (6 to 20) of large oval or ameboid nuclei; in some forms these break up into numerous nuclear fragments. The hypodermis also has a closed "lacunar" system of longitudinal and transverse vessels, probably

for distribution of nutrients absorbed from the host. These structures are confined to the trunk.

One of the striking things about Acanthocephala is the small number of nuclei; after an acanthocephalan reaches its final host there is no further cell division except in germ cells, even though the body may grow to hundreds of times its original size.

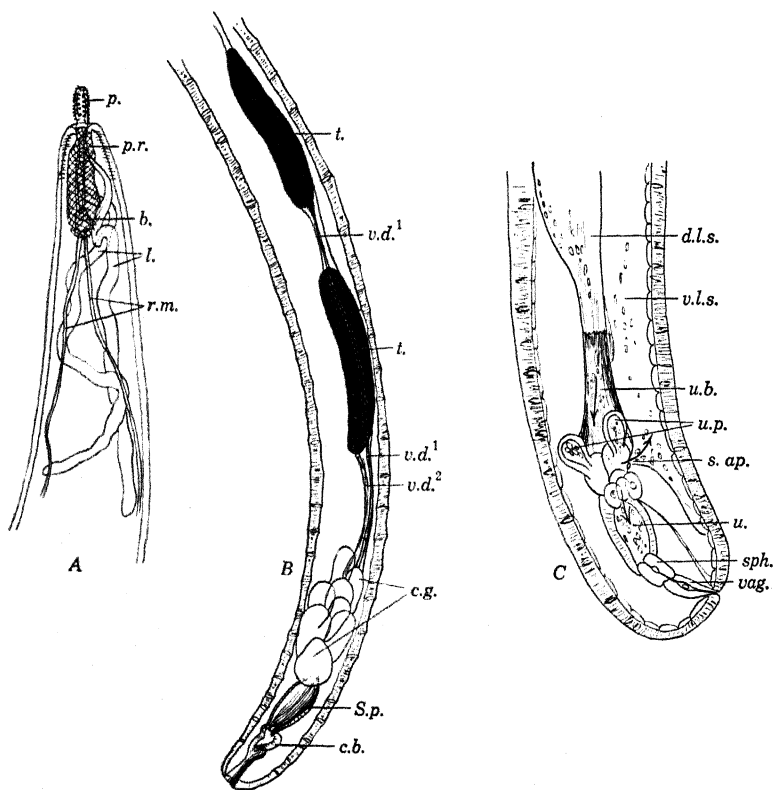


FIG. 110. *Moniliformis dubius*: A, anterior end; B, posterior end of ♂; C, posterior end of ♀; b., brain; c.b., copulatory bursa; c.g., cement glands; d.l.s., dorsal ligament sac; l., lemnisci; p., proboscis; p.r., proboscis receptacle; r.m., retractor muscles; s.ap., sorting apparatus; S.p., Saeftigen's pouch; sph., sphincter; t., testes; u., uterus; ut.b., uterine bell; u.p., uterine pouches; vag., vagina; v.d.¹ and v.d.², vasa deferentia; v.l.s., ventral ligament sac.

The sexes are separate, and the males are nearly always smaller than the females. The reproductive organs in both sexes are located in the posterior part of the trunk, and are enclosed by connective tissue *ligament sacs*. These are hollow tubes, extending most of the length of the body cavity of the trunk, single in males and in females of the order

Palaeacanthocephala, but divided into dorsal and ventral ones, communicating anteriorly, in females of the other orders. The males (Fig. 110*B*) have two testes, behind which are cement glands, usually 4 to 8 large unicellular glands but sometimes a syncytial mass. Behind the cement glands in some Acanthocephala is a sac-like structure called Saeftigen's pouch, through which, in most Acanthocephala, run the sperm ducts and ducts from the cement glands before they unite at its posterior end. At the posterior end of the worm there is a muscular bursa which can be protruded or retracted into the body.

In females (Fig. 110*C*) an ovary is present only in early stages of development, later breaking up into masses of cells which continue to multiply and produce ova. These float free in the ligament sacs, being retained in the dorsal one in the Eo- and Archi-acanthocephala, but liberated into the general body cavity by a disintegration of the single sac in the Palaeacanthocephala. Near the posterior end is a complicated structure called a uterine bell, into the wide-open anterior end of which the eggs are drawn. It acts as a sorting device; the smaller immature eggs are returned to the body cavity or into the ventral ligament sac through lateral openings, while the mature eggs are passed back through an oviduct to the posterior genital opening. The eggs, when ripe, contain a mature embryo called an acanthor surrounded by three envelopes, the outer of which often has shapes or markings useful in identification.

Life Cycle. The life cycle involves an intermediate host, which is usually an arthropod: small Crustacea for parasites of aquatic vertebrates; grubs, roaches, etc., for those of land animals. When the embryonated eggs (Fig. 111*A*) are swallowed, the spindle-shaped acanthor (Fig. 111*B*), usually armed with rostellar hooks and small body spines, hatches and bores into the intestinal wall, eventually reaching the body cavity. Meanwhile it grows and undergoes a gradual transformation; as development proceeds, the proboscis, proboscis sac, lemnisci, and rudiments of the sex organs are laid down. For this series of stages (Fig. 111*C, D*) leading up to the infective form Van Cleave applied the name "acanthella." A number of workers have applied this name to the fully developed infective larva, and Moore (1946) applied the name "preacanthella" to the earlier pre-infective stages, but Van Cleave insists that his name acanthella should apply only to these pre-infective stages, and that the infective form should be called a "juvenile." Since, however, "juvenile" is also applied to the re-encysted forms in secondary transport hosts, a new name is needed for the fully developed infective form. For this the name "cystacanth" is here proposed. The cystacanth (Fig. 111*E*) is enclosed

in a delicate hyaline sheath produced by the larva. The proboscis is fully formed but inverted, and the reproductive organs are sufficiently developed so that the sex is easily recognized. In *Moniliformis* larvae the hypodermis is expanded into broad flanges.

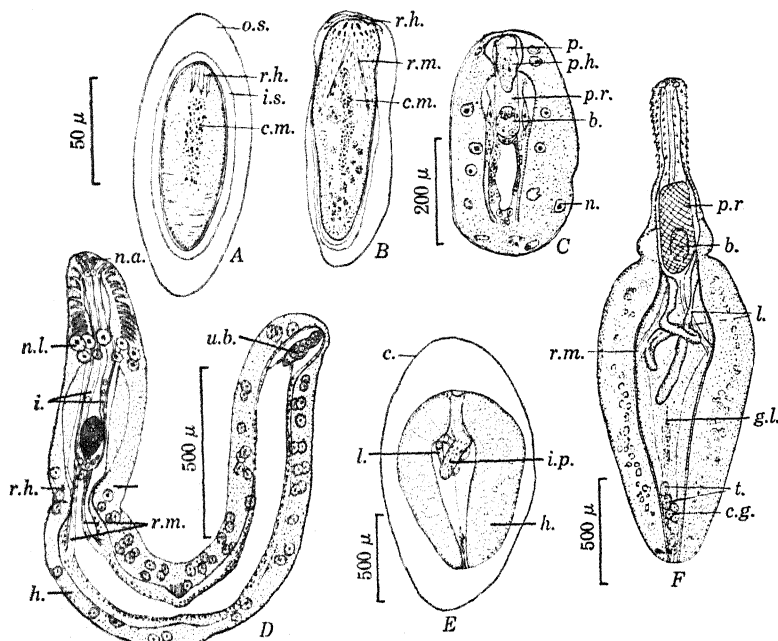


FIG. 111. Life cycle of *Moniliformis dubius*: A, egg; B, acanthor in process of escaping from egg shell and membranes; C, median sagittal section of larva from body cavity of roach 29 days after infection; D, acanthella dissected from enveloping sheath, about 40 days after infection; E, cystacanth from body cavity of roach, with proboscis inverted, about 50 days after infection; F, cystacanth freed from cyst and proboscis evaginated. Abbreviations: b., brain; c.g., cement glands; c.m., central nuclear mass; g.l., genital ligament; h., hypodermis; i., inveter muscles; i.p., inverted proboscis; i.s., inner shell; l., lemnisci; n., subcuticular nucleus; n.a., nuclei of apical ring; n.l., nuclei of lemniscal ring; o.s., outer shell; p., proboscis; p.h., developing proboscis hooks; p.r., proboscis receptacle; r.h., rostellar hooks; r.m., retractor muscle; t., testes; u.b., uterine bell. (After Moore, *J. Parasitol.*, 1946.)

Effects on Host. Acanthocephala damage their hosts principally by local injury and inflammation at the point of attachment of the spiny proboscis. When the worm moves and reattaches, the old sore may become infected by bacteria. Occasionally the worms cause perforation of the gut wall and precipitate a fatal peritonitis. In heavy infections, loss of appetite and interference with digestion may lead to unthriftiness. Dogs and coyotes infected with *Oncicola* (see p. 381) are said sometimes to develop rabies-like symptoms, suggesting the

possibility of transmission of a virus by the worms. Grassi and Calandruccio in 1888 reported acute pain and violent ringing in the ears experienced by the junior author 19 days after infecting himself with *Moniliformis* larvae.

Burlingame and Chandler (1941) showed that, as with some adult tapeworms, no true immunity to *Acanthocephala* is developed, resistance to reinfection being primarily a matter of competition for food and for favorable locations in the intestine.

Classification. The *Acanthocephala* constitute a small group of about a dozen families and about sixty genera which are quite widely divergent from other groups of worms but which are remarkably uniform among themselves, both in morphology and life cycle. Once placed in a single genus, *Echinorhynchus*, they were later (1892) divided into several families, then (1931) into two orders, which were expanded to three in 1936 and finally elevated by Van Cleave (1948) into a phylum containing two classes and four orders: class Metacanthocephala with the orders Palaeacanthocephala and Archiacanthocephala, and the class Eoacanthocephala with the orders Gyraacanthocephala and Neoacanthocephala.

To the writer the characters used by Van Cleave for differentiating these groups seem trivial. For example, in the table of characters given for distinguishing the orders, the only one in which the Gyraacanthocephala and Neoacanthocephala differ is the presence or absence of trunk spines, and even this character is variable in one of the other orders. No good character is presented for differentiating the two classes. For the present, therefore, we prefer to consider the *Acanthocephala* as constituting a single class with three orders, as proposed by Van Cleave in 1936, though we consider even this rather extreme.

1. **Palaeacanthocephala.** Proboscis hooks usually in long rows; spines present on trunk; nuclei in hypodermis usually fragmented; chief lacunar vessels in hypodermis lateral; single ligament sac in ♀ often breaks down; separate cement glands; eggs spindle-shaped, thin-shelled; mostly in fishes and aquatic birds and mammals, cystacanth in Crustacea.

2. **Eoacanthocephala.** Proboscis hooks usually in a few circles; trunk spines present or absent; nuclei in hypodermis few and large; chief lacunar vessels dorsal and ventral; distinct dorsal and ventral ligament sacs in ♀; syncytial cement glands; eggs ellipsoidal, thin-shelled; parasitic in fishes, except one in turtles, cystacanth in Crustacea.

3. **Archiacanthocephala.** Proboscis hooks either in long rows (e.g., *Moniliformis*) or in a few circles (e.g., *Oncicola* and *Macracanthorhynchus*); no spines on trunk; nuclei in hypodermis few and large; chief lacunar vessels dorsal and ventral; dorsal and ventral ligament sacs persist in ♀; separate cement glands; eggs usually oval, thick-shelled; protonephridia present in some; parasitic in terrestrial vertebrates, cystacanth in grubs, roaches, etc.

The only Acanthocephala found in man, *Moniliformis dubius* and *Macracanthorhynchus hirudinaceus*, belong to the Archiacanthocephala.

Moniliformis. The common spiny-headed worm of house rats, *Moniliformis dubius* (Figs. 110, 112A), has been found in man on a few occasions. Its body, 10 to 30 cm. long in females and 6 to 13 cm. in males, has annular rings which give it a tapeworm-like appearance.

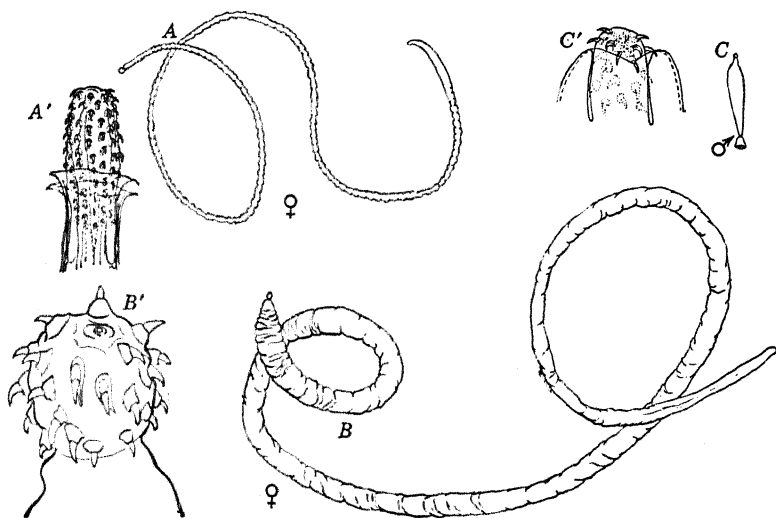


FIG. 112. Various Acanthocephala, adults drawn to same scale: A, *Moniliformis dubius* ♀; A', proboscis of same; B, *Macracanthorhynchus hirudinaceus*; B', proboscis of same; C, *Oncicola canis*; C', proboscis of same. (Adapted from various authors.)

It has a nearly cylindrical proboscis with 12 to 15 rows of vicious thorn-like hooks. It inhabits the small intestine of rats in many parts of the world. The eggs are over 100 μ in length. Cockroaches serve as intermediate hosts; the writer has found over 100 cystacanths in the body cavity of a *Periplaneta americana*. The eggs hatch in the mid-intestine of the roach, the liberated acanthors penetrating into the gut wall. By the tenth day they appear as minute specks on the outside of the intestinal wall, from which they eventually drop into the body cavity (Moore, 1946). The half-grown acanthella lies straight and has very broad ectodermal flanges (Fig. 111C), but with further development it bends V-shaped in its cyst (Fig. 111D), the body proper elongating and thickening until the flanges become inconspicuous. When fully developed, after 7 to 8 weeks, the cysts are about 1 to 1.2 mm. long and the cystacanths (Fig. 111F) 1.5 to 1.8 mm. long. In

Europe a beetle (*Blaps*) has been involved as an intermediate host, but the form found in wild rodents in Europe is not identical with that found in rats in the United States and South America.

Sandground (1926) found numerous immature specimens in the intestines of toads and lizards, where they had evidently attached themselves after being eaten with the intermediate hosts. Considering the propensity of *Acanthocephala* for re-establishing themselves as larvae in abnormal hosts, human infection might be possible without postulating the eating of roaches or beetles.

Macracanthorhynchus. The only other spiny-headed worm which has been recorded from man is the relatively huge species, *Macracanthorhynchus hirudinaceus* (Fig. 112B), commonly parasitic in pigs. This large worm, of which the females are 25 to 60 cm. long, though the males are only 5 to 10 cm., is pinkish and has a transversely wrinkled body which tapers from a rather broad, rounded head end to a slender posterior end. The presoma is relatively very small, with a little knob-like proboscis armed by five or six rows of thorns. The eggs are 80 to 100 μ long with sculptured brown shells; they are very resistant to desiccation and cold and remain viable in soil up to 3½ years. White grubs, the larvae of "June bugs," serve as intermediate hosts. The cystacanth is cylindrical and quite different in appearance from that of *Moniliformis*.

Lindemann in 1865 recorded this worm as parasitic in man among the peasants of the Volga Valley in southern Russia.

Other *Acanthocephala*. Aside from *Macracanthorhynchus* in pigs, the only *Acanthocephala* of importance to domestic animals are two genera, *Polymorphus* and *Filicollis*, which are injurious to ducks and geese. In both cases the intermediate hosts are Crustacea; *Polymorphus* takes advantage of an amphipod, *Gammarus*, and *Filicollis* of an isopod, *Asellus*. Dogs in Texas are sometimes infected with *Oncicola canis* (Fig. 112C), the larvae of which are commonly found in armadillos and sometimes in the walls of the esophagus of turkeys. An arthropod undoubtedly serves as a first intermediate host; it is an open question whether the second intermediate host is obligatory or merely convenient. Monkeys in zoological gardens infested with roaches sometimes suffer from *Prosthenorchis* infections, which are native in South American monkeys but spread to other species.

Treatment. Almost nothing is known about anthelmintics for *Acanthocephala*. Sodium fluoride given pigs to eliminate *Ascaris* does not affect *Macracanthorhynchus*. Lal performed some experiments on *Acanthocephala* of fishes *in vitro* and found that CCl_4 , CuSO_4 , and thymol killed at 0.05 per cent, but Santonin did not at 1 per cent.

Extract of male fern removed *Moniliformis* in an experimental human infection.

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The Nematodes in General

The nematodes constitute a large group of worms of comparatively simple organization, nearly all of which are total strangers to everyone but zoologists, although they play extremely important roles in the economy of nature. Popular ignorance of these animals is, as Cobb remarked, easy to understand since they are seldom if ever seen; they do not supply food, raiment, or other valuable material; they are not ornamental; they do not delight our ears with their songs or otherwise amuse us; and they fail even to furnish us with classic examples of industriousness, providence, or other virtues, although they might well be extolled by large-family enthusiasts. Thus avoiding the popular limelight, they do, nevertheless, unobtrusively leave their marks in the world. Probably every species of vertebrate animal on the earth affords harborage for nematode parasites, and Stoll (1947) estimated 2000 million human nematode infections in a world harboring 2200 million human inhabitants, a tribute, as he said, to the variety and biological efficiency of nematode life cycles. Only about a dozen species are important human parasites, although over fifty species have been known to make their homes in the human body occasionally.

Relationships. The nematodes constitute one of six classes included by Hyman (1951) in the phylum Nematelminthes (or Aschelminthes; see pp. 241-242). The majority of the estimated 500,000 species are free-living in soil or water, including the ocean; others, many closely related to these, have become parasitic in arthropods, mollusks, or plants. Some of the plant-parasitic forms do inestimable damage to crops. Most of the forms that are free-living or that find harborage in invertebrates or plants are barely visible to the naked eye, and are transparent enough so that every structure in the body can be observed as if in a glass model. These forms have very simple life cycles. The species parasitic in vertebrates, on the other hand, are often veritable giants, some up to several feet in length, and may have much more complicated life cycles.

The parasitic forms have without doubt evolved from more than one type of free-living form and do not, therefore, represent a single branch of the class Nematoda, which can properly be classified independently of the free-living forms. This, however, is what has been done in the past, for students of the nematodes parasitic in vertebrate animals had little knowledge or interest in the free-living forms. Only since about 1935 have attempts been made to reconcile these two estranged sections of the nematode clan.

General Structure. A typical nematode is an elongated, cylindrical worm, tapering more or less at head and tail ends, and encased in a very tough and impermeable transparent or semitransparent cuticle. This cuticle is not chitin, like the cuticle of arthropods, since it is sol-

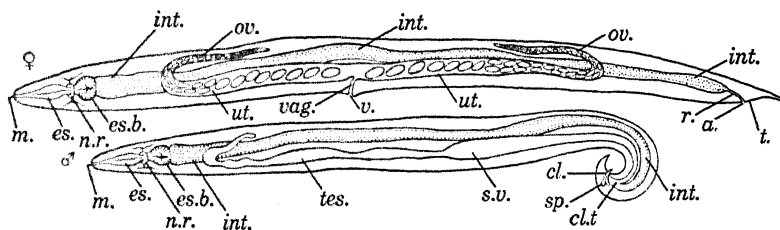


FIG. 113. Diagrams of ♀ and ♂ of free-living nematode of *Rhabditis* type; *a.*, anus; *cl.*, cloaca; *cl.t.*, cloacal tube; *es.*, esophagus; *es.b.*, esophageal bulb; *int.*, intestine; *m.*, mouth; *n.r.*, nerve ring; *ov.*, ovary; *r.*, rectum; *sp.*, spicules; *s.v.*, seminal vesicle and sperm duct; *t.*, tail; *tes.*, testis; *ut.*, uterus; *v.*, vulva; *vag.*, vagina.

uble in potassium hydroxide, but nematodes do have true chitin in the egg shells. Usually the cuticle is marked externally by fine transverse striations; it may have other inconspicuous markings and sometimes has bristles, spines, ridges, or expansions of various kinds. In some parasitic forms there are fin-like expansions in the neck region, in others in the tail region of the males, the latter commonly supported by fleshy papillae; they are known respectively as cervical and caudal alae. In the Strongylata there is a bell-shaped expansion at the posterior end of the males supported by fleshy rays conforming in number and arrangement to a definite plan; this is called a bursa. The cuticle is secreted by a protoplasmic syncytial layer called the hypodermis, in which no separate cells can be distinguished. Nuclei are present only in four thickened chords or "lines," one dorsal, one ventral, and two lateral. In these chords run nerve fibers and, in some species, canals connected with the excretory system.

Between the chords there is a single layer of longitudinally spindle-shaped muscle cells of very peculiar structure. In small transparent

worms the striated part of the muscle cell is limited to the part of the cell in contact with the hypodermis, and only a few, often only two, flat muscle cells are in each quadrant of a cross-section. In larger and more opaque worms, however, the muscle cells in each quadrant become very numerous and in cross-section have a flask-shaped appearance, with the striations along the "neck" of the flask as well as at the base of the cell (Fig. 114A). Worms with these two types of musculature are said to be "meromyarian" and "polymyarian," respectively, but there

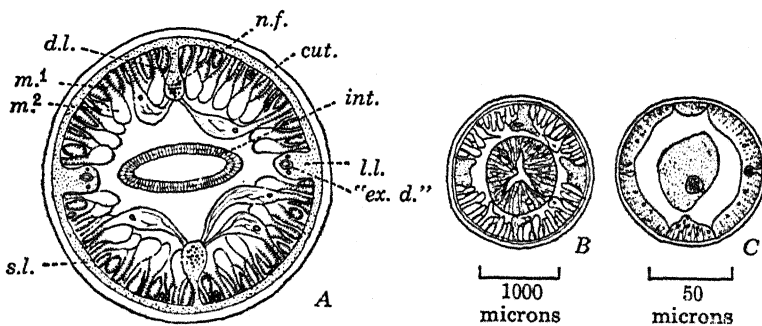


FIG. 114. A, cross-section of *Ascaris*, a polymyarian nematode, in prevulvar region; *cut.*, cuticle; *d.l.*, dorsal line; *ex.d.*, excretory duct; *int.*, intestine; *l.l.*, lateral line; *m.*¹, striated contractile portion of muscle cell; *m.*², protoplasmic portion of muscle cell; *n.f.*, nerve fibers. (After Brandes, adapted from Fantham, Stephens, and Theobald.) B, cross-section of esophageal region of *Ascaris*; C, of *Trichuris*. In *Ascaris* note the triangular lumen and thick muscular walls of the esophagus, and the numerous muscle cells in body wall. In *Trichuris* note the greatly reduced esophagus imbedded in the protoplasm of a large cell, and broad, flat muscle cells on body wall. (*Ascaris*, original; *Trichuris*, adapted from Chitwood.)

are all gradations between them. Contraction of these elongated muscles causes a twisting or bending of the body. Special muscles occur in the esophagus, ovejector, etc., and for moving the spicules of the male.

Between the muscles and the gut wall is a relatively spacious body cavity in which the reproductive organs lie, unattached except at their external openings. This cavity is not lined by an epithelium as is a true celome. It contains a fluid which serves as a distributing medium for digested food and for collection of waste products. It is provided with a small amount of "mesenterial" tissue and a few large phagocytic cells called celomocytes.

The nervous system consists of a conspicuous "nerve ring" around the esophagus, from which longitudinal nerve trunks run forward and backward. A few special sensory organs are present; at the anterior end are a pair of supposedly olfactory receptors called amphids, and

in some a similar pair, called phasmids, is situated on minute papillae behind the anus. These differ from ordinary tactile papillae in having canals connected with gland-like structures. There are tactile papillae about the mouth, a pair in the neck region of many forms (called deirids), and paired caudal or genital papillae in the males of many forms.

The excretory system is variable. Almost the only constant feature is a pore opening on the mid-ventral surface in the esophageal region; in some forms even this seems to be absent. A well-developed excretory system such as occurs in *Rhabditis* consists of an H-shaped system of tubes, the middle of the crossbar of the H being connected with the pore and the limbs lying in the lateral chords. In addition, two subventral gland cells open into the pore. In *Ascaris* the posterior limbs are well developed; in some the system is reduced to an inverted U or is developed on one side only. In some free-living nematodes the excretory system is reduced to a single glandular cell. Mueller in 1929 expressed the opinion that excretion takes place through the cuticle and that the so-called excretory system is really secretory. There is no circulatory system, and respiration is through the cuticle or possibly through the alimentary canal.

The mouth is variously modified. The primitive type in free-living nematodes is a simple opening surrounded by three lips, one dorsal and two lateroventral. This is retained by many groups of parasitic forms, including *Strongyloides*, oxyurids, and ascarids. In some forms, e.g., the filariae and their allies, the lips have disappeared, but in others two lateral lips, sometimes with a dorsal and ventral one also, have replaced the primitive three. In still others, especially some of the Strongylata, the mouth has been highly modified into a "buccal capsule," which may be supplied with such embellishments as crowns of leaf-like processes, cutting ridges, teeth, and lancets.

The mouth, or buccal capsule, leads into the digestive canal. This is a simple tube leading from the anterior mouth to an anus usually a short distance from the posterior end. It consists of two parts, an esophagus and an intestine. The esophagus has a chitinated triradiate lumen usually surrounded by muscle or gland cells (Fig. 114*B*), and ordinarily it has three esophageal glands embedded in its walls. In the suborder Trichurata, however, after a short anterior region the wall is greatly reduced and the lumen of the esophagus appears to pass like a capillary tube through a column of large cells (Figs. 114*C* and 115). Chitwood showed that these cells open by minute ducts into the esophagus, and he interprets them as reduplicated esophageal glands. This column of glandular cells is called a stichosome. Sometimes the pos-

terior end of the esophagus enlarges into a bulb provided with valves (Fig. 113).

The intestine is a flat or cylindrical tube, usually straight, and is lined by a single layer of cells (Fig. 114A). In some forms, like the strongyles, it is lined by only 18 to 20 cells in all, whereas in *Ascaris* there are about a million. At the posterior end there is a chitinated rectum. In females the intestine has a separate anal opening, but in males the intestine and reproductive system open into a common cloaca.

Reproductive Systems. With rare exceptions parasitic nematodes have separate sexes, which are externally distinguishable; usually the males are smaller, and they differ in the form of the tail. In one instance the male lives as a parasite in the vagina of the female! In both sexes the reproductive system consists primitively of long tubules, part of which serve as ovaries or testes and part as ducts (Fig. 113). In all parasitic nematodes the male system is reduced to a single tubule, but the female system is double with rare exceptions and in a few cases is further reduplicated. The inner ends of the tubules are fine, coiled, thread-like organs closed at the ends, which produce the cells that ultimately become eggs or sperms. These sex glands open directly into a continuous part of the same tube, usually larger in caliber, called the uterus or vas deferens, as the case may be. The walls of the uterus appear to supply the yolk and shell material for the egg.

In the male the single vas deferens usually has an enlargement or seminal vesicle, followed by a muscular ejaculatory duct which opens into the cloaca. Males normally have a pair of sclerotized "spicules," which lie in pouches dorsal to the ejaculatory duct near the cloaca. They are capable of exertion and are used to guide the sperms into the vagina of the female at the time of copulation. There may be a third smaller sclerotized body or accessory piece called a gubernaculum. The size and shape of the spicules vary greatly in different kinds of nematodes and are often very useful in identification. In a few forms one or both spicules may be missing.

In the females of simple types of nematodes the two uteri come together near the middle of the body and open into a single vulva (Fig. 113). In most parasitic forms, however, the uteri first unite into a common tube, the vagina. Frequently the vagina or the branches of the uteri have enlarged, thin-walled chambers which serve as seminal receptacles, and also muscular ovejectors which by a peristaltic action force the eggs through to the vulva one at a time. The vulva in different species may vary in position from just behind the mouth to a point just in front of the anus.

Development and Life Cycle. The development of nematodes is a comparatively simple process. The original egg cell, after being enclosed in a membrane or shell, segments into 2, 4, 8, 16, etc., cells, until it forms a solid morula. This then begins to assume a tadpole shape and become hollow inside, and then proceeds to form an elongated embryo provided with a simple digestive tract. After ten consecutive cell divisions, in the later ones of which not all the cells participate each time, the definitive form of the first larval stage is reached. Thereafter development proceeds more slowly and, as in insects, is punctuated by a series of molts, normally four, although in some forms one or two molts may occur in the egg before hatching. Although the successive stages differ in details of structure they are never totally unlike each other.

The state of development at the time the eggs are deposited varies greatly, apparently depending upon different oxygen requirements for development. Some leave the mother's body unsegmented (*Ascaris* and *Trichuris*); some in early stages of segmentation (hookworms and their allies); some in the tadpole stage (*Enterobius*), and some as fully developed embryos (*Trichinella*, *Strongyloides*, and filariae). Usually no further development occurs until the eggs or embryos have reached a new environment, either outside the body or in an intermediate host, except in the case of *Trichinella*, the embryos of which find *their* new environment in the muscles of the parental host. Having reached this new environment the embryo, either inside the egg or after hatching from it, commonly undergoes two molts, reaching the third stage, before it is infective for another definite host. When it has reached that stage it ceases to grow or develop until transfer to a new host is accomplished.

The simplest type of life cycle is that in which the embryonated eggs are swallowed by the host. The embryos, usually in the third stage, hatch in the intestine and may develop to maturity there, only burying themselves temporarily in the mucous membranes, e.g., *Enterobius* and *Trichuris*, or they may make a preliminary journey through the host's body via heart, lungs, trachea, and esophagus, and thus back to the intestine, e.g., *Ascaris*. This life cycle may be modified by the first-stage embryos hatching outside the body and growing and developing to the infective stage as free-living larvae, then re-entering the definitive host by burrowing through the skin, e.g., hookworms, or being swallowed with vegetation, e.g., *Haemonchus*.

Strongyloides reproduces parthenogenetically and may intercalate a generation of morphologically different free-living males and females. *Trichinella* produces embryos which penetrate into the host's body and encyst in the muscles to await being eaten by another host, thus

substituting the original host for the outside world as a place for preliminary partial development. The filariae and their allies (suborder Spirurata) substitute insects or other invertebrates as a place for partial development, thus requiring a true intermediate host. A few, e.g., *Gnathostoma*, require two intermediate hosts, the larvae developing first in a *Cyclops*, continuing in a fish or other cold-blooded vertebrate, and reaching sexual maturity in a mammal. Some nematodes, after having reached an infective stage, can re-encyst if they get into an unsuitable host.

The methods of escaping from and re-entering a final host vary in accordance with the modifications in the life cycle.

Classification. The classification of nematodes is still in a very unsettled state. This is partly due to the process of promoting nematode groups to higher ranks as more and more species are described. Families or even genera of a few years ago are now superfamilies, suborders, or orders, according to the willingness of helminthologists to recognize the promotions. The classification has been subjected to a veritable earthquake by attempts, which must sooner or later be recognized, to combine the classification of free-living and parasitic groups in a single coordinated whole. Chitwood has done most in reconciling these two estranged groups and has evolved a classification which embraces them both, but Chitwood's conclusions will probably have to undergo some ripening and confirmation before parasitologists in general will accept this New Deal in nematode classification.

In the first place, he divides the entire class into two subclasses, Phasmodia and Aphasmodia, for the fundamental characters of which the student is referred to Chitwood and Chitwood. The Phasmodia include the majority of soil nematodes, as well as most of the forms parasitic in insects and vertebrates, whereas the Aphasmodia include mainly aquatic forms and a few parasitic ones—the Trichurata, mermithids, and Dioctophymata. The further division of these subclasses into orders involves some unfamiliar names, which may not survive the limelight of publicity, so we omit them and give only the more or less familiar suborders and superfamilies. As an *ad interim* classification the following is suggested:

Subclass **Aphasmodia**. No phasmods (caudal sensory organs); amphids much modified externally except in parasitic forms; excretory system rudimentary or absent; celomocytes and mesenteric tissue well developed.

1. Suborder **Trichurata**. Esophagus a very long, fine tube embedded for most of its length in a column of glandular cells; females with one ovary; males with one spicule or none. Includes *Trichuris*, *Trichinella*, and *Capillaria*.
2. Suborder **Dioctophymata**. Large worms; esophagus cylindrical; female

with one ovary; male with one spicule and a terminal sucker; no excretory system. Includes kidney worm (*Dioctophyma*).

Subclass **Phasmidia**. Phasmids present; amphids simple pores; excretory system present, not rudimentary; celomocytes (6 or less) and mesenterial tissue weakly developed.

1. Suborder **Rhabditata**. Small, transparent, meromyarian worms; esophagus usually with one or two bulbs; mouth simple or with 3 or 6 minute lips or papillae; no specialized ojectors, and vagina transverse; majority free-living, some with an alternating generation of parthogenetic parasitic females. Includes *Rhabditis* and *Strongyloides*.

2. Suborder **Ascaridata**. Esophagus bulbed or cylindrical; vagina elongate; mouth usually with 3 or 6 lips; males usually with 2 spicules; tail of male not spirally coiled but usually curled ventrally; no true bursa, but alae may be present.

Superfamily 1. **Ascaridoidea**. Cervical papillae present; mostly large, stout polymyarian worms; males with 2 spicules; tail curled ventrally, with or without lateral alae; esophagus muscular, with or without a bulb. Includes *Ascaris* and *Heterakis*.

Superfamily 2. **Oxyuroidea**. Cervical papillae absent; mostly small or medium-sized transparent meromyarian worms; males with 1 or 2 spicules; esophagus bulbed; tail of female usually slender and pointed. Includes *Enterobius*.

3. Suborder **Strongylata**. Usually meromyarian; males with 2 spicules and with a true bursa supported by 6 paired rays and one dorsal one which may be divided; mouth simple, without lips, or with a buccal capsule; esophagus muscular, club-shaped, or cylindrical; eggs thin-shelled and colorless. Includes hookworms, strongyles, gapeworms, and lungworms.
4. Suborder **Spirurata**. Esophagus cylindrical, often part glandular and part muscular; males usually with 2 spicules and well-developed alae and papillae on spirally coiled tail; mouth either simple with no or rudimentary lips, or with 2 or 4 paired lips; vagina elongated and tubular; posterior part of esophagus with numerous nuclei; require intermediate host.

Superfamily 1. **Spiruroidea**. Mouth usually with a chitinated vestibule and 2 or 4 paired lips; vulva usually in middle or posterior part of body; males with spirally coiled tail with broad alae supported by papillae; eggs usually escape with feces and are eaten by intermediate host. Includes *Gongylonema*, *Gnathostoma*, and *Physaloptera*.

Superfamily 2. **Filarioidea**. Slender, delicate worms; mouth usually simple, without lips and rarely a vestibule; females with vulva far anterior; males small with coiled tails with or without alae, but always with papillae; usually give birth to embryos which swarm in blood or skin and develop in bloodsucking insects. Includes filariae (*Wuchereria*, *Onchocerca*, etc.).

5. Suborder **Camallanata**. Mouth simple or with lateral jaws; posterior part of esophagus with 1 or 3 large nuclei; requires intermediate host.

Superfamily 1. **Dracunculoidea**. Mouth simple, surrounded by circlet of papillae; alimentary canal and vulva atrophied in adult females; males much smaller than females; embryos evacuated through burst uterus and mouth. Includes guinea worm (*Dracunculus*).

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Trichuris, *Trichinella*,
and Their Allies

SUBORDER TRICHURATA

The worms belonging to the suborder Trichurata differ strikingly from all other nematodes in the appearance of the esophagus, which consists of a fine capillary tube embedded in a long column of single cells which form a structure called a stichosome, and which are believed to function as esophageal glands. The anterior portion of the body, containing only the esophagus, is always very fine and slender and in some forms is sharply demarcated from the relatively coarse posterior part of the body containing the intestine and reproductive organs. The vulva opens either at the end of the esophagus or anterior to this point. The eggs, if produced, are easily recognizable by their barrel shape with an opercular plug at each end. *Trichinella*, however, forms no egg shells, and the embryos hatch before birth.

The families and principal genera of this suborder are differentiated as follows:

Trichuridae. ♀ oviparous; ♂ with protrusible spiny spicular sheath and usually a spicule.

Trichuris. Anterior portion of body much more slender than posterior; whipworms.

Capillaria. Anterior portion slender but not sharply different from posterior; fine, hairlike worms.

Trichinellidae. ♀ viviparous; ♂ with no spicule or spicule sheath; contains *Trichinella* only.

Trichosomoididae. ♀ oviparous; ♂ parasitic in vagina of ♀; in urinary bladder of rodents; 1 genus, *Trichosomoides*.

***Trichuris* or Whipworms**

The whipworm derives its name from its whip-like form, having a thick posterior part of the body containing the reproductive organs and a longer lash-like anterior part occupied only by the slender esophagus. The name *Trichuris* means "thread tail" and was given before it was

recognized that the slender part was really a head and not a tail. Someone else more appropriately named the worm *Trichocephalus* (thread head), but since the other name was given first it must be used, in spite of its reflection on the inaccurate observation of its originator.

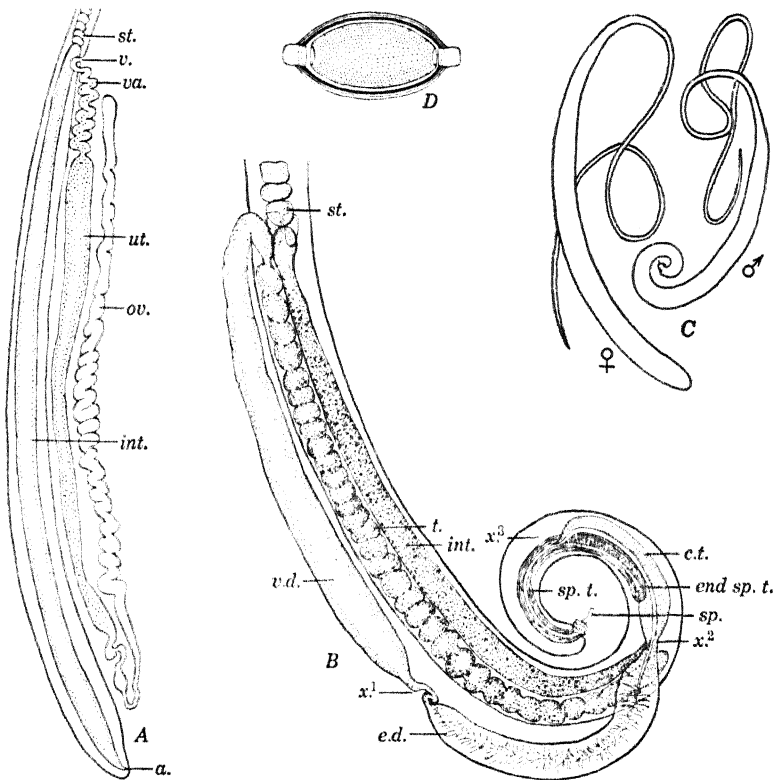


FIG. 115. Human whipworm, *Trichuris trichiura*. A, female, and B, male, dissected and organs spread, $\times 15$; C, body shapes of male and female, $\times 4$; D, egg, $\times 50$. Abbreviations: a, anus; c.t., cloacal tube; e.d., ejaculatory duct; int., intestine; ov., ovary; ut., uterus; v., vulva; va., vagina; v.d., vas deferens; x.¹, junction of vas deferens and ejaculatory duct; x.², junction of ejaculatory duct and intestine to form cloacal tube; x.³, junction of cloacal tube and spicular tube.

Whipworms are common inhabitants of the cecum and large intestine of many animals, including dogs, rodents, pigs, and all sorts of ruminants, as well as man and monkeys. Schwartz concluded in 1928 that the whipworms of pig and man are identical and that the whipworm commonly found in apes and monkeys is also the same species. The human species, *Trichuris trichiura*, has a world-wide distribution and is

very common in the moist parts of warm countries. It usually inhabits the region of the cecum and appendix but sometimes lives in the sigmoid and rectum also. It buries its slender head in folds of the intestinal wall, occasionally threading it into the mucous membranes.

Morphology. The whipworm has a length of 30 to 50 mm., of which the thread-like esophageal portion occupies about two-thirds. The mouth has no lips but is provided with a minute spear. The males are a little smaller than the females and can be distinguished by the curled tail end of the body (Fig. 115C). They have a single long spicule, retractile into a sheath with a spiny, bulbous end. Unlike the condition in most nematodes, the ejaculatory duct (distal part of the sperm duct) joins the intestine a long way from the anus, forming a cloacal tube. This joins the spicular tube, containing the spicule and its sheath, also at some distance from the anus (Fig. 115B). The vulva of the female (Fig. 115A) is at the junction of the two parts of the body; the single uterus contains many of the barrel-shaped eggs (Fig. 115D), which measure about 50 by 22 μ and are unsegmented when they leave the host.

Life Cycle and Epidemiology. The life cycle is very simple. The eggs develop slowly; even when kept moist and warm they require 3 to 6 weeks for the embryo to reach the hatching point, and under less favorable conditions they may be delayed for months or even years. The eggs are less resistant to desiccation than are those of *Ascaris*, and nearly all die within 12 days when dried on a slide, even in a saturated atmosphere. Epidemiological evidence shows that a high incidence of *Trichuris* infection is always associated with an abundance of moisture in the soil, due either to a heavy and well-distributed rainfall or to dense shade. Infection may result from polluted water or from hand contaminations from polluted moist soil. In the United States *Trichuris* infections are more "spotty" in distribution than *Ascaris* and occur abundantly only in places where there is more or less doorway pollution, dense shade close to the houses, a heavy rainfall, and a dense clay soil to conserve the moisture. These conditions are met in southwestern Louisiana and in the southern Appalachians.

When embryonated eggs are swallowed they hatch near the cecum, the embryos burrow into the villi for a few days, and then take up their residence in the cecum, where they mature in about a month. The worms live for a number of years, and therefore infections build up gradually and do not show seasonal fluctuations.

Pathology. *Trichuris* infections often produce no obvious symptoms, since frequently only a few worms are present, but sometimes the whole lower part of the colon and rectum may have a film of squirm-

ing *Trichuris*. Such heavy infections may be suggestive of severe hookworm disease. Symptoms observed are loss of appetite, nausea, diarrhea, blood-streaked stools, weakness, loss of weight, anemia, eosinophilia, abdominal discomfort, emaciation, and sometimes fever. Prolapse of the rectum is common in chronic cases. According to Jung and Beaver (1951) symptoms may always be expected when the egg count is 30,000 per cc. or over, indicating several hundreds of worms; in undernourished children the pathogenic threshold is undoubtedly lower. Kourí and Valdez Dias (1952) report massive infestations in children 1 to 5 years old in Cuba, in whom the vomiting, diarrhea, and emaciation may cause death. In mild cases Swartzwelder (1938) found abdominal discomfort or pains, suggestive of appendicitis, to be the commonest symptom. Jung and Beaver (1951) found a remarkably high association of *Trichuris* and *Entamoeba histolytica* infections in children in Louisiana.

Treatment. *Trichuris* is a particularly difficult worm to expel because of its position in the cecum, remote from either the mouth or the anus. Most anthelmintics given by mouth are relatively ineffective, although good results have been obtained with fresh or refrigerated latex of certain figs (*Ficus*), called by the Spanish name, lèche de higuerón. Jung and Beaver recommended enemas of 0.2 per cent hexylresorcinol in water or glycerin solution; 500 to 700 cc. is given slowly after a cleansing enema, and retained for 30 minutes. Kourí also recommended hexylresorcinol enemas. A simpler but less effective treatment is a mixture of tetrachlorethylene (2.7 cc.) and oil of chenopodium (0.3 cc.) by mouth for adults, less for children, followed by a saline purge in 2 hours. "Enseals" of emetin hydrochloride have also been recommended.

Other Trichuridae

Species of the genus *Capillaria*, with slender, delicate body and relatively short esophageal portion, are parasitic in a wide variety of vertebrates and exercise a remarkable choice of habitats.

Capillaria hepatica lives in the liver of rats and other rodents, where its eggs accumulate in dry, yellow patches. Since the eggs require air to become embryonated, direct eating of the egg-burdened liver does not cause infection; the egg must first be liberated and exposed to air by decomposition of the original host or preliminary passage through the intestine of a predatory animal. Several valid human cases and a number of pseudo-infections in which the eggs were presumably eaten with livers of infected animals have been recorded.

Another species, *C. (or Eucoleus) aerophila*, occurs in the respiratory

system of cats, dogs, etc.; it is an important parasite of foxes, causing more harm than all other infections combined, except distemper. One human case has been reported from Moscow. Other species live in the esophagus and crop or in the intestine of birds, in the stomach of rats, in the urinary bladder of cats and foxes, and in the intestines of many animals.

The life cycles of most species are essentially the same as the life cycle of *Trichuris* except for migration via the blood stream of species living outside the alimentary canal. *C. annulata*, infecting the esophagus and crop, and *C. caudinflata*, infecting the intestine of chicks and turkeys, add an additional chapter, for the eggs fail to become infective until after ingestion by earthworms, which serve as true intermediate hosts (Morehouse, 1944). Consequently the fondness of poultry for earthworms is often penalized by *Capillaria* infection.

Trichinella spiralis and Trichiniasis

The trichina worm, *Trichinella spiralis*, though an intestinal parasite as an adult, is quite different in significance from other intestinal worms. The serious and often fatal results of trichiniasis are due to the offspring of the infecting worms and not to the adult worms in the intestine. Without a doubt this worm, with the pork tapeworm as an accomplice, was responsible for the old Jewish law against the eating of pork. Unlike most human helminths, this one is almost entirely absent from the tropics; it is primarily a parasite of Europe, the United States, and arctic regions, with moderate infection in Mexico and southern South America, particularly Chile; it is practically absent from San Francisco to Suez and from Africa and Australia. In the arctics Rausch found trichinosis prevalent not only in Eskimos, polar bears, and dogs, but also in marine mammals such as seals and white whales, which constitute a large proportion of the natural food of man and dogs. How the fish-eating marine mammals get infected is an unsolved problem.

Structure and Life History. The trichina worm infects many animals. In America hogs are most commonly infected, and infection is common in rats which have access to waste pork. Cats are frequently infected, dogs less often. Man is highly susceptible, and many rodents are easily infected if fed trichinized meat. Birds are very resistant.

The worms gain entrance to the digestive tract as larvae encysted in meat (Fig. 118). They are freed from their cysts in the stomach or intestine and penetrate into the mucosa of the small intestine. Here they undergo a series of molts which bring them to the adult stage. They may reach sexual maturity and copulate as early as 40 hours after

being swallowed. The females (Fig. 116) are 3 to 4 mm. long, whitish, slender and tapering from the middle of the body toward the anterior end; the males are only 1.5 mm. long. The long capillary esophagus occupies one-third to one-half the length of the body. In the female the vulva opens near the middle of the esophageal region; the anterior part of the uterus is crowded with embryos, whereas the posterior part contains developing eggs. The males, aside from their minute size, are characterized by the presence of a pair of conical appendages at the posterior end. In both sexes the anus (or cloaca) is terminal. The males have no spicule (Fig. 116C).

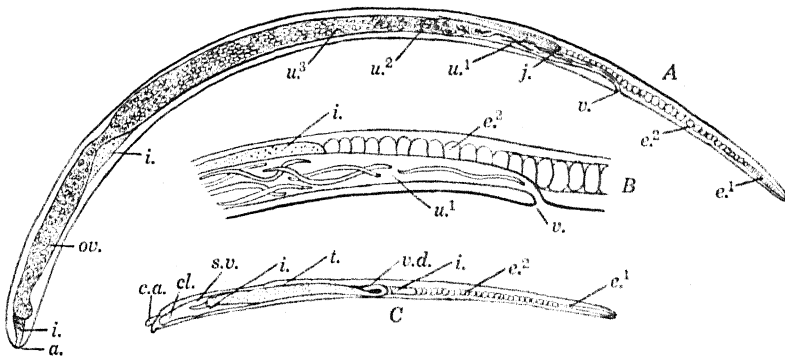


FIG. 116. Adult *Trichinella spiralis*. A, female; B, vulva region of female; C, male; a., anus; c.a., caudal appendages; cl., cloacal tube; e.¹, anterior portion of esophagus; e.², posterior portion of esophagus or stichosome; i., intestine; j., junction of esophagus and intestine; ov., ovary; s.v., seminal vesicle; t., testis; u.¹, anterior portion of uterus with free embryos; u.², middle portion of uterus with embryos coiled in vitelline membrane; u.³, posterior portion of uterus with ova; v., vulva; v.d., vas deferens. Entire worms $\times 40$ in length, width $\times 80$.

The adult intestinal worms are essentially short-lived, usually disappearing within 2 or 3 months after infection. Many males pass out of the intestine soon after mating, though some live as long as the females.

Trichina embryos develop in the uterus of the mother and are scarcely 0.1 mm. in length when born. The mother worms usually burrow into the mucous membranes far enough so that the young can be deposited in the tissues rather than into the lumen of the intestine. Embryos may be born within a week after the parents have been swallowed by the host and are most numerous in the circulating blood between the eighth and twenty-fifth days after infection.

The embryos enter lymph or blood vessels in the intestinal wall and are distributed over the entire body. They have been found in practi-

cally every organ and tissue but undergo further development inside the cells of the voluntary muscles. Active muscles containing a rich blood supply, such as those of the diaphragm, ribs, larynx, tongue, eye, and certain ones in the limbs, are particularly favored, but all the striated muscles in the body except the heart muscle are liable to invasion. Unlike many tissue-penetrating larvae, however, trichina embryos do not pass through the placenta and cause prenatal infections.

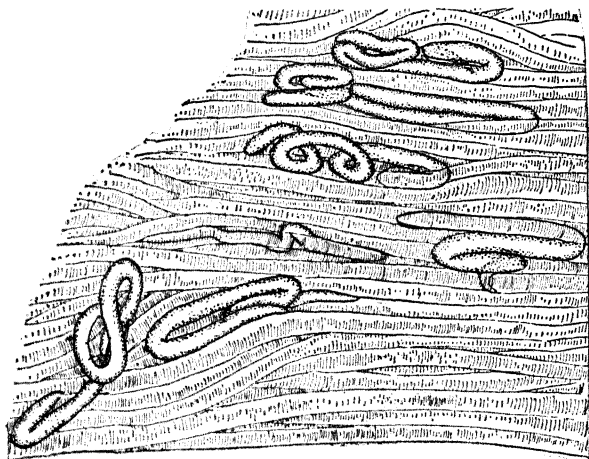


FIG. 117. Larvae of trichina worm burrowing in human flesh before encystment. From preparation from diaphragm of a victim of trichiniasis. $\times 75$.

After entering muscle fibers the worms grow rapidly to a length of 1 mm., ten times their original size, and become sexually differentiated. They finally roll themselves into a spiral and are infective after about 17 or 18 days.

The inflammation caused by the movements and waste products of the worms results in the degeneration of the enclosing muscle fibers and in the formation of cysts around the young worms, beginning about a month after infection. The cysts (Fig. 118), at first very delicate but gradually thickening, are lemon-shaped, 0.25 to 0.5 mm. long, lying parallel with the muscle fibers; they are not fully developed until after 7 or 8 weeks. As a rule only one or two worms are enclosed in a cyst but as many as seven have been seen.

After 7 or 8 months or sometimes much later, the cyst walls start to calcify, beginning at the poles. After 18 months or longer the entire cyst becomes calcified and appears as a hard calcareous nodule. Even the enclosed worm, which usually degenerates and dies after some months, becomes calcified after a number of years. At times, however,

the trichina worms do not die and disintegrate so soon and the calcification process is much slower. Experimentally the calcification of well-formed cysts can be hastened by administration of calcium and ergosterol or even more by large doses of parathormone.

Estimates of the number of encysted larvae that may be expected per female worm vary greatly, but experimental work with various animals indicates about 1500. An ounce of heavily infected sausage may contain more than 100,000 encysted larvae, over half of which are

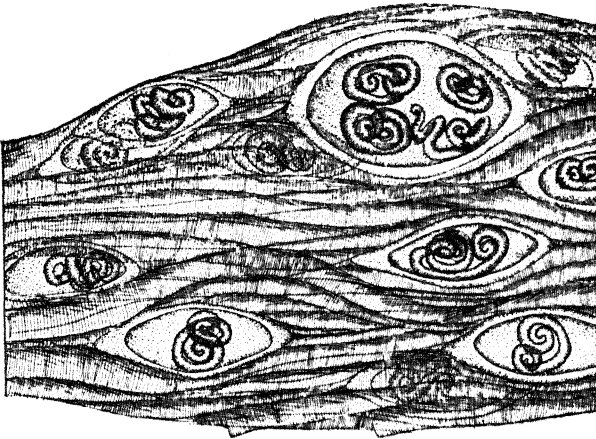


FIG. 118. Larvae of trichina worms, *Trichinella spiralis*, encysted in striated muscle fibers in pork. Camera lucida drawing of cysts in infected sausage. $\times 75$.

females, so the eating of it may result in more than a hundred million larvae distributing themselves throughout the body of the unfortunate victim. It has been estimated that for man ingestion of 5 trichina larvae per gram of body weight is fatal, for hogs 10, and for rats 30.

After encysting in the flesh no further development takes place until the flesh is eaten by a susceptible animal, whereupon the worms mature and begin reproducing in a few days. It will be seen that, whereas most worms begin the attempt to find new hosts at the egg or early embryo stage of the second generation, the trichina worm does not make a break from its parental host until it has reached the infective stage for another host.

Mode of Infection and Prevalence. Obviously man usually becomes infected from eating raw or imperfectly cooked infected meat, in most cases pork. Under modern conditions hogs undoubtedly are most commonly infected by being fed on garbage containing pork scraps, as Hall pointed out in 1937. Nearly 40 per cent of cities of

over 4500 population and 50 per cent of cities of over 15,000 dispose of garbage by feeding it to hogs. Stoll suggested calling *Trichinella* the "garbage worm."

Rats appear to play a very minor role in the epidemiology as compared with infected pork scraps, for hogs are not by nature rat-eaters; Hall says that in his experience hogs and rats usually live together on very friendly terms. Rats pass the disease among themselves by cannibalism, but in most cases it is a closed circuit.

Hall showed that the prevalence of the infection in both man and hogs is closely correlated with methods of raising hogs in different parts of the country. It is highest on the North Atlantic seaboard and in California, where hogs are most extensively fed on garbage. In the Middle West, where a higher percentage are raised on pastures and fed on corn, the incidence is lower and it is still lower in the South where the hogs are generally allowed to roam the fields and woods, competing with the squirrels for acorns and without easy access to kitchen scraps or city garbage.

The incidence of human infection is astonishingly high; where examinations have been made in routine autopsies the infection ranges from about 5 per cent in New Orleans to 18 to 27 per cent in northern and western cities, with a general average of over 16 per cent in the entire United States; even these figures are apparently below the actual incidence. Stoll in 1947 called attention to the fact that the United States has three times as much trichiniasis as all the rest of the world combined. The incidence in hogs in this country is about 1.5 per cent; at this rate, as Gould (1945) pointed out, an average pork-eating American might eat 200 meals of trichinous pork in his lifetime, so the 16 per cent infection is not so surprising. Fortunately, in contrast to this high incidence of infection, outbreaks since 1900 have been mild, with low mortality; less than 600 clinical cases a year are reported, with a mortality of less than 5 per cent.

The most serious outbreaks occur among Germans, Austrians, and Italians who are fond of various forms of uncooked sausage and "wurst." Nearly all serious outbreaks can be traced back to animals slaughtered on farms or in small butchering establishments, since in sausage made in large slaughterhouses the meat of an infected animal is almost certain to be diluted with the meat of uninfected animals. Moreover, in federally inspected establishments pork destined for raw consumption is refrigerated long enough to destroy the infection (see below). There is a particularly high death rate among rural school teachers and preachers, who are invited by their hospitable neighbors to sample and praise new batches of delicious, freshly made sausage.

The Disease. As we have seen, the vast majority of human infections are never diagnosed or suspected unless the diaphragms are examined microscopically or by artificial digestion after death. Hall and Collins call attention to the fact that in not one of 222 infections found post-mortem had a diagnosis of trichiniasis been made, although in some there were almost 1000 worms per gram of muscle, and no person harboring that many worms could by any stretch of the imagination be considered free of symptoms. Clinical symptoms are certainly far commoner than the number of reported cases would indicate. Some cases are mistaken for typhoid, ptomaine poisoning, "intestinal flu," or what not, but in many cases the patients probably just didn't feel well. The severity of the symptoms is largely dependent on the number of living worms eaten, although it is undoubtedly influenced also by the general state of health and resistance and by immunity due to prior infections.

The clinical course of trichiniasis is very irregular. Characteristically, the first symptoms are diarrhea, abdominal pains, nausea, and other gastro-intestinal symptoms, with or without fever, flushing, etc., caused by irritation of the intestine by the growing and adult worms burrowing into its walls. There is often a sort of general torpor accompanied by weakness, muscular twitching, etc. As the larvae become numerous in the blood and tissues, eosinophilia develops, in extreme cases reaching 50 per cent and even 90 per cent.

The second stage is the period of migration of larvae and penetration of muscles; it is frequently fatal. One of the earliest symptoms in this stage is a marked puffiness under the eyes and in the lids. The characteristic symptoms are intense muscular pains and rheumatic aches. Disturbances in the particular muscles invaded cause interference with movements of the eyes, mastication, respiration, etc. The respiratory troubles become particularly severe in the fourth and fifth weeks of the disease, in fact sometimes so severe as to cause death from dyspnea or asthma. Profuse sweating and more or less constant fever, though sometimes occurring in the first stage also, are particularly characteristic of the second stage. The fever is commonly absent in children. Eosinophilia and leucocytosis are nearly always present.

The third stage, accompanying the encystment of the parasites, begins about 6 weeks after infection. The symptoms of the second stage become exaggerated, and in addition the face again becomes puffy, and the arms, legs, and abdominal walls are also swollen. The patient becomes anemic, skin eruptions occur, the muscular pains gradually subside, and the swollen portions of the skin often scale off. Pneumonia is a common complication. In fatal cases death usually comes

in the fourth to sixth week, rarely before the end of the second or after the seventh.

Numerous variations from this course involve both omissions and additions. In America a more or less persistent diarrhea accompanied by eosinophilia, fever, puffy eyes, and muscular pains should always suggest trichiniasis. Sometimes the characteristic symptoms are overshadowed by others, involving the heart, eye, or nervous system, where the larvae burrow but do not develop. Sometimes even the gastrointestinal symptoms fail to appear, and when there are accompanying bacterial infections there may be no eosinophilia.

Recovery usually does not occur in less than 5 to 6 weeks after infection and often not for several months. Recurrent muscular pains and weakness may continue for a year. Commonly cases in which a copious diarrhea appears early in the disease are of short duration and mild in type. Young children, owing either to smaller quantities of pork eaten or to greater tendency to diarrhea, are likely to recover quickly.

Diagnosis. To confirm a diagnosis is not easy. Search for adult worms in feces is unreliable, and larvae in blood or cerebrospinal fluid, though present after 8 to 10 days, are difficult to find. The removal of a bit of muscle and examination of it pressed out between two slides is of no use early in the infection but is often diagnostic later.

Bachman (1928) devised a skin test and a precipitin test which have proved helpful. The antigen consists of dried and powdered larvae obtained by artificial digestion of the meat of heavily infected animals. In positive skin tests a blanched wheal appears in 5 minutes and reaches a diameter of 1 to 2 cm. in an hour. This test is seldom positive before about 11 to 14 days, however, and may remain positive for at least 7 years after infection, so might be misleading. It may, however, be put to practical use in the detection of infected hogs (see below). Bozicevich et al. (1951) have developed an easy 15-minute flocculation test in which *Trichinella* antigen is adsorbed on bentonite particles, which then clump on a slide when exposed to serum containing antibodies. After 2 weeks negative tests are valuable in ruling out trichiniasis, whereas positive ones are valuable as corroborative evidence. Positive reactions sometimes occur in *Trichuris* infections. In view of the difficulty in making a correct diagnosis, it is not surprising that trichiniasis has been mistaken for at least fifty other disease conditions.

Treatment. The search for a good anthelmintic to kill the larvae in the muscles has not yet been very fruitful, and little progress has been made in expelling the adult worms from the intestine. On the basis

of success in experimental animals, both Hetrazan and piperazine citrate show promise of effectiveness in removing adult *Trichinella* from man; of piperazine Chou and Brown (in 1954) suggested daily doses of 2 to 3 grams.

Often, however, diagnosis is not made until the critical stage, when millions of embryos are migrating through the body and developing in muscle fibers. The treatment employed then can be only symptomatic.

Immunity. Considerable resistance to infection is produced by prior exposure. McCoy showed that this resistance was effective against worms developing in the intestine as well as larvae migrating parenterally. This has been confirmed by Bozicevich and Detre (*NIH Studies in Trichinosis*, VIII, 1940), who found antigen in blood of rabbits 24 hours after they were fed trichina larvae, and by Zaiman (1953, 1954), who found uninfected members of parabiologic twins showing heightened resistance to reinfection when the twins were separated 5 days after infection of one member, before any parenteral larvae were present, and also when the mate was infected with worms rendered incapable of reproduction by x-rays. Roth (1943) obtained some degree of immunity by infecting animals with larvae of one sex only. In immunized mice the worms of subsequent infections show the characteristic evidences of immunity found in other worm infections (see pp. 23-24)—small worms, retarded development, and greatly inhibited reproduction.

A far smaller degree of protection results from injection of vaccines or immune serum. When either adults or larvae are placed in immune serum a precipitate forms at mouth and anus, as in the case of *Nippostrongylus* (see p. 23). This seems to uphold the writer's idea, expressed in 1939, that the immune reaction is directed mainly against the nutritional enzymes or their metabolic products. This is further supported by Campbell's (1954) demonstration that resistance of mice to *Trichinella* infection can be enhanced by injection of secretions and excretions of *Trichinella* larvae.

From the evidence available it may be presumed that human beings may often be protected from the ill effects of eating heavily trichinized meat by having eaten more lightly infected meat at some earlier date. Data are lacking, however, on how long the immunity is effective.

Prevention. Personal preventive measures against trichiniasis are easy and consist simply in abstinence from all pork that is not thoroughly cooked. Trichinae are quickly destroyed by a temperature of 55°C. (131°F.), but pork must be cooked for a length of time proportionate to its weight in order to insure the permeation of heat to the center. At least 30 to 36 minutes' boiling should be allowed to each

kilogram of meat (2¼ lb.). Hurried roasting does not destroy the parasites as long as red or raw portions are left in the center.

Augustine (1933) showed that quick cooling to $-34^{\circ}\text{C}.$, or quick cooling to $-18^{\circ}\text{C}.$, followed by storage at that temperature for 24 hours, or at $-15^{\circ}\text{C}.$ for 48 hours, renders the trichinae non-infective. Cold storage for 20 days at a temperature of $-15^{\circ}\text{C}.$ is required by the U. S. Bureau of Animal Industry for pork products to be used uncooked, unless cured in accordance with certain specified processes, but this appears to be an unnecessarily long time. Salting and smoking are not efficacious unless carried out under certain conditions.

Prevention by examination of meat for larvae was thought by Stiles to be too expensive, too incomplete, and inapplicable to the most dangerous sources of infection—hogs butchered on farms or small local establishments. In Chile, however, examination of compressed samples of pork, projected on a screen, has been found inexpensive, rapid, and effective in discovering all but very light infections, which are not dangerous.

The most feasible and practical plan for the control of trichiniasis consists in forbidding the feeding of raw garbage to hogs, as has been done for years in Canada and England. It would be better to stop raising hogs on garbage altogether, but in the United States 1,500,000 hogs are raised annually wholly or in part on commercial garbage. This practice is responsible for the spread of a number of other hog diseases as well, especially cholera, foot-and-mouth disease, and vesicular exanthema. In 1952 a nationwide outbreak of the last caused heavy losses to hog raisers, and did more than did 25,000,000 human *Trichinella* infections to persuade the swine industry to look upon legislation directed against feeding raw garbage to hogs with a less jaundiced eye. Since that outbreak thirty-seven states either have initiated such legislation or are preparing to do so. For interstate traffic the Public Health Service requires that garbage be steamed or boiled for 30 minutes before being fed to hogs.

Other Aphasmidia

SUBORDER DIOCTOPHYMATA. THE GIANT KIDNEY WORM

The only aphasmid nematodes other than the Trichurata which are normally parasitic in vertebrates are the Dioctophymata. The females have one ovary, anterior vulva (in *Dioctophyma*), and terminal anus; the males have a terminal bell-shaped bursa without rays, and a single spicule (Fig. 119A). The eggs have thick, pitted shells.

The only species of importance is *D. renale*, the giant kidney worm,

found in the pelvis of the kidney or in the abdominal cavity of mink, dogs, and occasionally in many other animals, including man (Fig. 119B). It is a huge, blood-red worm, the female of which sometimes exceeds 3 ft. in length, with the diameter of a small finger, whereas the male may be 6 to 16 in. long.

It is usually the right kidney that is infected; this swells to several times its size and eventually becomes a mere shell, often with a bony plate developed on its dorsomedial surface (McNeil, 1948). The left kidney hypertrophies to about twice its normal size. It has generally

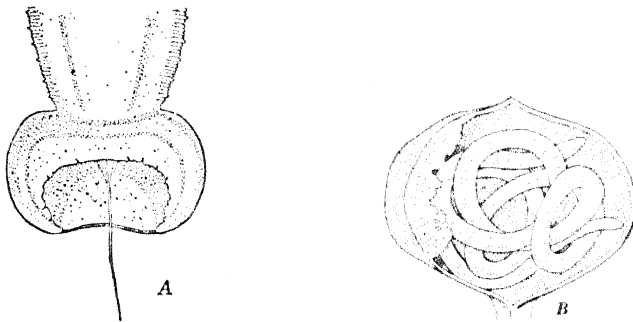


FIG. 119. *Diocotophyma renale*, giant kidney worm. A, copulatory bursa of ♂, ventral view, with bristle-like spicule projecting; B, adult worm in kidney of a dog. (A, after Stéfansky, *Ann. Parasitol.*, 6, 1928. B, adapted from Railliet.)

been assumed that the parasite invades one of the kidneys first and enters the abdominal cavity after the kidney has been more or less destroyed, but Stéfanski and Strankowski (1936) think that it develops in the body cavity and later penetrates the kidney by means of a histolytic secretion from its highly developed esophageal glands.

Woodhead (1945) reported a remarkable life cycle for this worm involving a first stage of development in a leech parasitic on crayfish and a second one in a fish, *Ameiurus melas* (bullhead), before reaching the adult stage in a mammal. The stages described are strikingly similar to those of the Gordiacea (see p. 242).

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• 19 •

The Hookworms and Their Allies Suborder Strongylata

No group of the nematodes causes more injury to man or greater economic loss through attacks on his domestic animals than the members of the suborder Strongylata, the great majority of which are parasites of mammals. Many are bloodsuckers and cause severe injury to their hosts by loss of blood sucked by them or wasted from hemorrhages; the result is anemia, loss of vitality, and general unthriftiness.

The worms of this suborder have one easily recognizable character which is constant and peculiar to them, namely, a bursa surrounding the cloaca of the male. This is a sort of umbrella-like expansion of the cuticle at the end of the body which is supported by fleshy rays comparable with the ribs of an umbrella. The arrangement of the rays is remarkably constant, and each ray is given a name. Usually the bursa consists of three lobes, two lateral and one dorsal, and it may or may not be split ventrally; it varies in size, and in some of the lung worms (*Metastrongylidae*) it is vestigial or even absent. The dorsal lobe is supported by a dorsal ray which may be bifurcated only at its tip or may be split almost to the base; from its root there arise a pair of externo-dorsal rays which usually enter the lateral lobes. The latter are supported by three pairs of lateral rays arising from a common root, and two pairs of ventral rays arising from another common root. The names and arrangement of these rays as they occur in hookworms are shown in Figs. 120 and 122*A* and *C*.

Other characteristics of the group are the club-shaped or cylindrical muscular esophagus and the absence of distinct lips; the mouth is either a simple opening at the end of a fine slender head or is provided with a more or less highly specialized buccal capsule. The eggs always have thin transparent shells that do not become bile stained and are therefore colorless. They are in some stage of segmentation or contain embryos when laid. The eggs hatch outside the body into free-living

larvae which, after reaching a certain stage of development, enter a new host either by burrowing through the skin or by being ingested with water or vegetation, or in the case of some of the lungworms, with an intermediate or transport host.

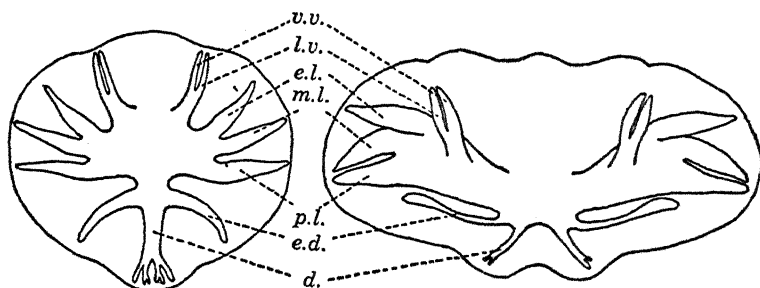


FIG. 120. Diagrams of bursas (spread out flat) of *Ancylostoma duodenale* (left) and *Necator americanus* (right), showing arrangement of rays; d., dorsal ray; e.d., externo-dorsal; e.l., externo-lateral; l.v., latero-ventral; m.l., medio-lateral; p.l., postero-lateral; v.v., ventro-ventral. (After Chandler, *Hookworm Disease*, 1929.)

The suborder, on the basis of work by Dougherty (1945, 1951) may be classified into families as follows:

- I. Eustomatous forms, i.e., with well-developed mouth capsule.
 1. **Ancylostomidae** (hookworms). Capsule with ventral teeth or plates inside opening (Fig. 121).
 2. **Strongylidae**. With crown of leaf-like processes (corona radiata) (Fig. 128).
 3. **Syngamidae** (gapeworms). Capsule hooped by large chitinous ring (Fig. 130).
- II. Meiostomatous forms, i.e., with reduced or vestigial mouth capsule.
 1. **Trichostrongylidae**. Intestinal forms with ovejectors (Fig. 132B); bursa well developed. No intermediate hosts.
 2. **Metastrongylidae**. Lungworms: vulva posterior, vagina long, and uteri parallel (Fig. 132A), except in a few forms in carnivores (*Skrjabiniinae*) and one genus, *Dictyocaulus*, in ruminants; bursa reduced; intermediate hosts (mollusks or annelids) required except by *Dictyocaulus*.

Hookworms of Man

Importance. Until recently hookworm ranked without question as the most important helminthic infection of man, but it has been brought under control in many countries to such an extent in the last few decades that now it is quite likely the schistosomes that deserve first place. Hookworm is never spectacular like some other diseases, but is essentially insidious; year after year, generation after generation,

it saps the vitality and undermines the health and efficiency of whole communities. For years the "poor white trash" of some rural parts of our South were considered a shiftless, good-for-nothing, irresponsible people, worthy only of scorn and of the sordid poverty and ignorance which they brought upon themselves as the fruits of their supposedly innate shiftlessness, but the discovery that these unfortunate people were the victims of hookworms which stunted them physically and mentally made them objects of pity rather than scorn. Fortunately, their lot has been enormously improved since the early part of the present century.

Distribution. Hookworm infection exists where local conditions are favorable in most tropical and subtropical parts of the world, bounded approximately by the thirty-sixth parallel in the north and the thirtieth parallel in the south. In North America it occurs in the southeastern United States west to eastern Texas and north to Virginia, Kentucky, southwestern Missouri, and Arkansas; in Mexico, principally on the Gulf Coast from southern Tamaulipas to the base of the Yucatan peninsula; and in most of Central America and some of the West Indies, especially Puerto Rico. In South America it is present over vast areas east of the Andes and south to the River Platte, especially in the Amazon Valley and southeast coast of Brazil. In the Old World it occurs mainly in Egypt, west and central Africa south to Natal, and Madagascar; northern coast of Asia Minor and irrigated areas in the Middle East; parts of India, Burma, China, Japan, Indo-China, Malaya, East Indies, Borneo, New Guinea, some of the Polynesian Islands, and the Queensland coast.

Surveys by Keller, Leathers, et al. (1940) showed a remarkable decrease in both the incidence and intensity of infection in the United States since the first surveys were made about 20 years earlier. In six of eight southern states the average incidence, by techniques that miss very light cases, was 36.6 per cent in 1910-1914 and 11.2 per cent in 1930-1938. In 1940 the incidences varied from 50 per cent in western Florida to 7 to 9 per cent in Tennessee and Kentucky, the areas of important infection being largely localized. The highest incidence is in whites in the 15- to 19-year age group. Today only a small percentage of those infected have enough worms to cause clinical symptoms.

Species. Two species of hookworms are common human parasites, *Ancylostoma duodenale* and *Necator americanus*. They are similar in general appearance and in most details of their life cycle, habits, etc., but *A. duodenale* is much more injurious to its host and is harder to expel by means of anthelmintics. All hookworms, including many species found in dogs, cats, herbivores, and other animals, are rather

stocky worms, usually about half an inch in length, with a well-developed bursa, very long, needle-like spicules, and with a conspicuous goblet- or cup-shaped buccal capsule, guarded ventrally by a pair of chitinous plates which either bear teeth, as in the ancylostomes, or have a blade-like edge, as in the necators and their allies (Fig. 121). The human ancylostome, *A. duodenale*, has two well-developed teeth on each plate, with a rudimentary third one near the median line (Fig. 121A). *A. caninum*, common in dogs and cats, has three pairs of

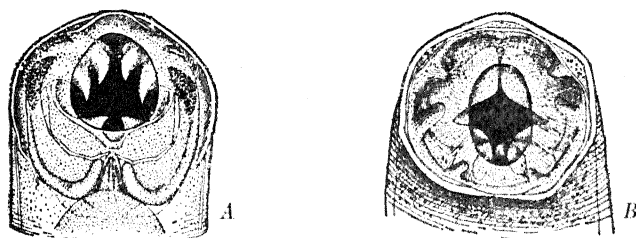


FIG. 121. Mouth and buccal cavity of *Ancylostoma duodenale* (A), and *Necator americanus* (B), showing teeth in former and cutting ridges in latter. Dorsal view. A, $\times 100$; B, $\times 230$. (Adapted from Looss.)

teeth (Fig. 123C), and *A. braziliense* and *A. ceylanicum*, also common in cats and dogs, especially in the tropics, have one large tooth and a rudimentary one on each side. These species were confused with each other until Biocca (1951) showed clear differences between them both in mouth capsules and in bursas (Fig. 123A, B, D, and E).

ANCYLOSTOMA. *Ancylostoma duodenale* (Fig. 122) is primarily a northern species and predominates only in Europe, North Africa, western Asia, northern China, and Japan, but it has accompanied infected mankind to all parts of the world; it is possible that it may have been the original species in at least a part of the American aborigines. It is larger and coarser than *Necator*, the females averaging about 12 mm. and the males about 9 mm. in length. Freshly expelled specimens have a dirty rust color. The vulva of the female is behind the middle of the body, and the tail is tipped by a minute spine. The males are easily recognizable by their broad bursas, which have the rays arranged as shown in Figs. 120 and 122A. The single dorsal ray and the nearly equal spread of the three lateral rays are good marks for distinguishing this species from *Necator*, but after a little experience the two genera of either sex can be distinguished with the naked eye by the form of the head, which in ancylostomes is coarse and only slightly bent dorsally, whereas in necators it is much finer and sharply bent (Fig. 122). The structure of the mouth capsule of this species is shown in Fig. 121.

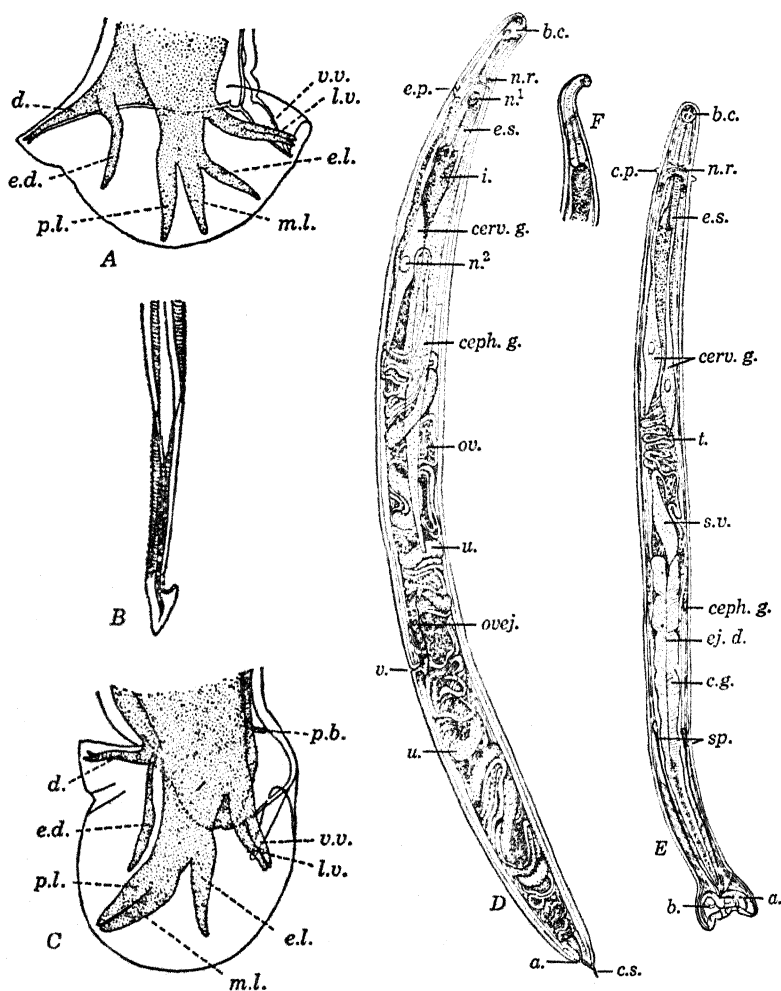


FIG. 122. Hookworms of man. A, bursa of *Ancylostoma duodenale*; B, tip of spicules of *Necator*; C, bursa of *Necator americanus* (abbreviations as in Fig. 120); D, ♀ *Ancylostoma duodenale*; E, ♂ of same; F, head of *Necator americanus*, same scale as D and E. Abbreviations: a., anus; b., bursa; b.c., buccal capsule; ceph.g., cephalic gland; cerv.g., cervical gland; c.g., cement glands; c.p., cervical papilla; c.s., caudal spine; e.p., excretory pore; ej.d., ejaculatory duct; es., esophagus; i., intestine; n.¹, nucleus of cephalic gland; n.², nucleus of cervical gland; n.r., nerve ring; ov., ovary; ovej., ovejector; sp., spicules; s.v., seminal vesicle; t., testis; u., uterus; v., vulva. (Adapted from Looss.)

A. duodenale is primarily a human parasite but on rare occasions has been found in pigs and experimentally can be reared occasionally in dogs, cats, and monkeys.

A. ceylanicum, according to Biocca, is found in Asia and South America, and is an occasional human intestinal parasite in southeast Asia. *A. braziliense* occurs in Africa and South America. It is common in dogs and cats on the Gulf Coast of the United States, and is the cause of creeping eruption in that area (see p. 421).

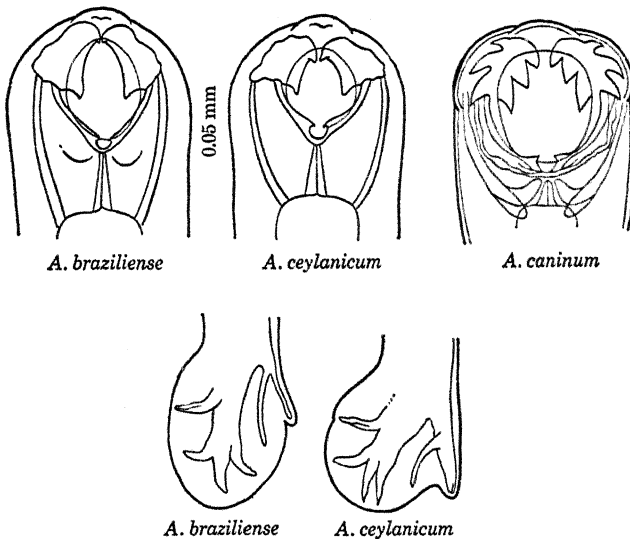


FIG. 123. Mouth capsules and bursas of *Ancylostoma braziliense*, *A. ceylanicum* and *A. caninum*. Comparing *A. braziliense* and *A. ceylanicum*, note in former smaller accessory tooth in mouth capsule, not directly on contour; longer lateral rays of bursa; longer trunk of lateral rays and these rays all divergent; and more slender externodorsal ray arising nearer base of dorsal ray. (Figures of *braziliense* and *ceylanicum* after Biocca, J. Helm., 1951.)

NECATOR. *Necator americanus* is primarily a tropical worm. It is now the predominant species in all parts of the world except those mentioned in the section on ancylostomes. In our southern states 95 per cent or more of the hookworms are of this species. It is often called the "American" hookworm because it was first discovered here, but it is probably African in origin. Interesting evidence of past and present migrations of mankind can be traced in the hookworm fauna of various countries and islands.

Necator is smaller and more slender than *A. duodenale*; the females average 10 to 11 mm. in length and the males 7 to 8 mm. The vulva

of the female is anterior to the middle of the body, and there is no caudal spine. The bursa is longer and narrower than in the ancylostomes (Figs. 120 and 122C), and is distinguished by the split dorsal ray and approximation of two of the lateral rays. The structure of the mouth capsule is shown in Fig. 121B. *N. americanus* is primarily a human parasite, though capable of development in apes and monkeys, but the same or a very similar form has been found in pigs in tropical America. Other species of *Necator* have been described from chimpanzees.

Life Cycle. The adult hookworms of both genera reside in the small intestine, where they draw a bit of the mucous membrane into their buccal capsules and nourish themselves on blood and tissue juices which they suck (Fig. 124). Their main business in life is the production of



FIG. 124. *Necator americanus*; section showing manner of attachment to intestinal wall. (Adapted from Ashford and Igaravidez, from photograph by W. W. Gray.)

eggs, and they tend strictly to business! Careful estimates show that each female necator produces 5000 to 10,000 eggs per day, and ancylostomes over twice that many. Yet the bodies of the worms contain on the average only about 5 per cent of this number of eggs at any one time.

The eggs (Fig. 125, 1 and 2) average about 70 by 38 μ in necators and 60 by 38 μ in ancylostomes, but the species cannot be identified reliably by eggs in the feces. They are in the four-celled stage when freshly passed and do not develop further until exposed to air.

They require moisture and warmth also, and, if these conditions are present and there are no injurious substances in the feces, an embryo hatches in less than 24 hours. Usually feces in the tropics are not left undisturbed but are stirred up, aerated, and mixed with soil by dung beetles and other insects, which greatly improves the environment for the eggs and larvae of hookworms.

The hatched larvae (Fig. 125, 8) are of the "rhabditiform" type, i.e., they have an esophagus with an anterior thick portion connected by a neck-like region with a posterior bulb, a character which distinguishes these larvae from "strongyliform" larvae, which have a long cylindrical esophagus with a terminal bulb that is not sharply demarcated. After the second molt the larvae of hookworms lose their typical rhabditiform esophagus, and become strongyliform. The free-living larvae of hookworms in all stages are distinguishable from the rhabditi-

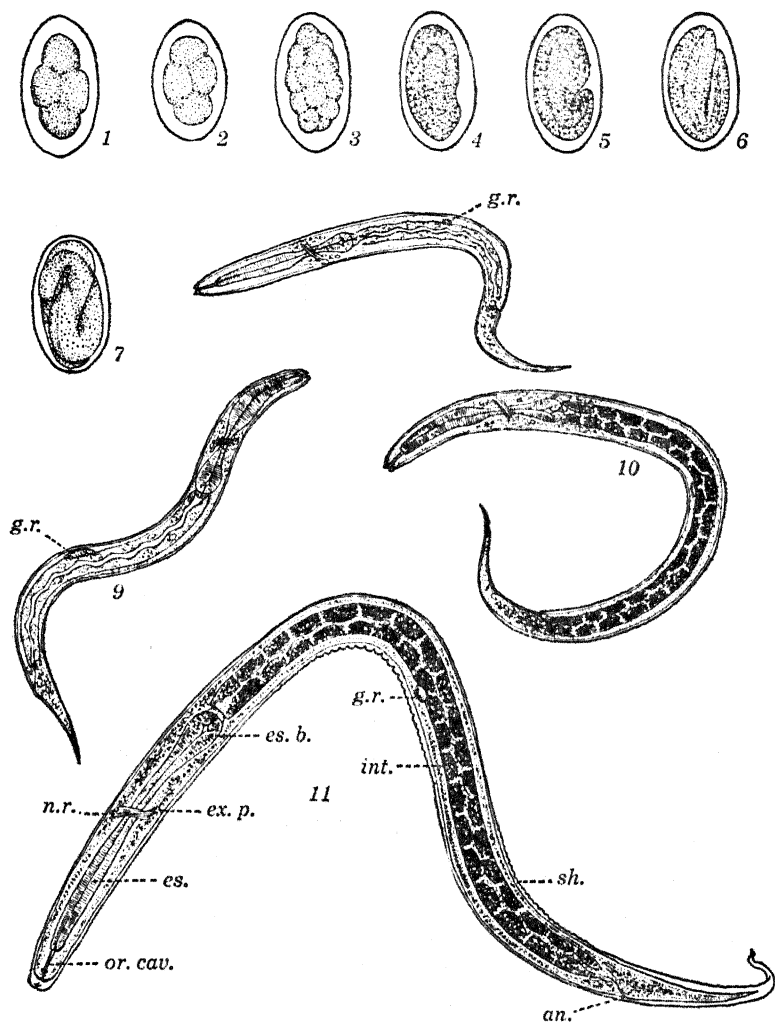


FIG. 125. Stages in life cycle of hookworms from egg to infective larva. 1, egg of *Necator americanus* at time of leaving body of host; 2, same of *Ancylostoma duodenale*; 3 to 7, stages in segmentation and development of embryo in the egg; 8, newly hatched embryo; 9, same of *Strongyloides* for comparison (note difference in length of oral cavity and size of genital rudiment, *g.r.*); 10, second stage larva; 11, third stage (infective) larva; *an.*, anus; *ex.p.*, excretory pore; *g.r.*, genital rudiment; *int.*, intestine; *n.r.*, nerve ring; *es.*, esophagus; *es.b.*, esophageal bulb; *or.cav.*, oral cavity; *sh.*, sheath. $\times 285$. (After Looss from Chandler, *Hookworm Disease*, 1929.)

form larvae of *Strongyloides* by the long mouth cavity (cf. Figs. 125, 8 and 9). Larvae of many Strongylata of domestic animals, e.g., esophagostomes and trichostrongyles, are distinguishable by their long, filamentous tails.

The larvae feed on bacteria and perhaps other matters in the feces, and grow rapidly. At the end of about 2 days they molt, grow some more, and at the end of about 5 days they molt again. This time, however, the shed cuticle is retained as a protecting sheath (Fig. 125, 11), which may remain until the larva penetrates the skin of a host or may be torn or worn away by the movements in the soil. A small oval body, the genital primordium (Fig. 125, 11, g.r.), is visible near the middle of the body. These larvae are easily distinguishable from the more typically filariform infective larvae of *Strongyloides* (Fig. 136) by the shorter and bulbed esophagus and the pointed tail (notched in *Strongyloides*).

These larvae are now in the infective stage. They eat no more but subsist on food material stored up as granules in the intestinal cells during their 5 days of feasting. The optimum temperature for development is between 70° and 85°F.; lower temperatures retard and finally stop it, and in frosty weather the eggs and young larvae are destroyed; higher temperatures decrease hatching and increase larval mortality. The infective larvae of hookworms are about 500 to 600 μ in length, with characteristic form, color, and movements which make them recognizable after some experience. Minute details of anatomy also make it possible to distinguish necator from ancylostome larvae.

Biology of Larvae. Hookworm larvae normally live in the upper half inch of soil, and commonly climb up to the highest points to which a film of moisture extends on soil particles, dead vegetation, etc., and extend their bodies into the air to await an opportunity to apply themselves to a human foot which is unfortunate enough to come in contact with them. When exposed to a hot sun or to superficial drying of the soil they retreat into crevices in the upper layer.

They do not migrate laterally to any great extent, but are dispersed by rain, insects, etc. In loose-textured soil they can migrate vertically, even to the extent of 2 or 3 ft., but in trenches or pits they do not climb the walls, since, from the standpoint of the larvae, the soil walls are very rugged paths. Before they have climbed more than a few inches they reach the top of some projecting particle from which they extend themselves, unaware that they have not reached a vantage point at the top, and are thus trapped. The larvae are strongly attracted by moderate heat and are stimulated to activity by contact with objects;

it is these reactions which cause the larvae to burrow into the skin of animals.

Since the larvae have only the stored food granules on which to subsist until a suitable host is reached, the more active they are the sooner their food supply is used up and the sooner they die. Vertical migration through even a few inches of soil is an expensive process for them. Larvae that have had their reserve food greatly depleted, although still alive, may not have enough energy to penetrate the skin of a host.

Mode of Infection. Infection normally takes place by penetration of the skin by the larvae; this important discovery was first made by Looss in 1898 when he accidentally spilled some water containing larvae on his hands and acquired an infection. Skin penetration usually results from contact with infested soil, most frequently when the victim is barefooted, but mud containing larvae kicked against the ankles causes numerous light infections in well-shod people. Infection may also come from handling feces-soiled clothing, etc., if they are left damp 4 or 5 days before being laundered. Less frequently, infection results from water or food harboring the infective larvae. Larvae thus swallowed sometimes, though not commonly, develop without migration through the lungs.

The larvae burrow until they enter a lymph or blood vessel and are then carried by the blood stream to the right side of the heart and thence to the lungs, where they are usually caught in the capillaries and again proceed to burrow, this time into the air spaces of the lung. The ciliary movement of the epithelium of the bronchial tubes and trachea carries them to the throat, whence they are either expectorated with sputum or swallowed. If they are swallowed, they go to the intestine and bury themselves between the villi and in the depths of glands for a brief period until the third molt is completed, after which they acquire a provisional mouth capsule and can successfully adhere to the mucosa. The third molt may occur as early as 3 days after infection, but it may be delayed for several days longer. The larvae grow rapidly to a length of 3 to 5 mm. and then molt for the fourth and last time, with the acquisition of the definitive mouth capsule and the development of reproductive organs. In man the eggs first begin to appear in the feces usually about 6 weeks after infection.

Longevity. The length of life of the adult worms in the intestine may be 5 years or more but is much shorter for the majority of the worms. There is evidence that in natural infections, when repeated reinfections occur, the peak of egg production of newly acquired worms may occur after about 6 months, after which there is a rapid falling off in number of worms. A high percentage of newly acquired worms

in repeatedly infected individuals is probably lost within a year. In places where there are prolonged unfavorable seasons little cumulative increase in worms can occur on account of the large annual reduction in worms during the season when reinfection is largely stopped.

Epidemiology. Many environmental factors influence the amount of hookworm infection in a community. Temperature, as already intimated, is a prime controlling factor. Rainfall is also of fundamental importance. Heavy hookworm infections are never common in localities having less than 40 inches of rain a year, and with larger annual rainfall much depends on the seasonal distribution and on the distribution within each month, for hookworm larvae will not withstand complete desiccation.

When soil is drying, e.g., after a shower, or as feces dry up, some of the larvae escape desiccation by retreating under the surface of the soil ahead of the receding zone of free moisture, but many fail to do so and become victims of desiccation. Immediately following a rain the surviving larvae come to the surface and again many fail to escape when the surface dries; they are killed by desiccation long before the soil has lost its moist appearance. Beaver (1953) found that in soil wetted once a day the number of viable larvae fell off about 90 per cent within a week, whereas in soil which was not moistened and became dry and loose at the surface, most of the larvae lived many days longer. Probably extremely few larvae survive in tropical soils for more than 6 or 7 weeks. Excessive rainfall, resulting in saturated soil, may exert an even greater check on hookworm infection. Such local factors as humidity, drainage, and hygroscopic nature of the soil also influence the effect of intershower drying.

The nature of the soil is very influential; hookworm never thrives in regions of heavy clay soil, whereas in adjoining areas with sandy or humus soil it may constitute an important problem. Salt impregnation of soil is also injurious. Vegetation exerts an influence, since dense shade is far more favorable for the development and longevity of larvae than light shade or exposure to sun. Irrigation may make rainless regions favorable for hookworm if moistened soil is selected for defecation.

Animals, such as pigs, dogs, and cattle, which devour feces, especially in the tropics, exert an influence, since in pigs and dogs the eggs in fresh feces pass through the animals uninjured and may be voided with the feces of the animals in places where they are more, or less, likely to cause infection. In chickens, on the other hand, and probably in cattle also, most of the eggs are destroyed when ingested. Insects play an important role. Dung beetles are allies of hookworms since they

mix feces with soil and render the cultural conditions more favorable; cockroaches, on the other hand, destroy most of the eggs in their "gizzards" and were found by the writer to play an important part in keeping down hookworm infections in Indian mines.

Many human factors also affect the amount of hookworm. Some races are more susceptible than others. The white race is particularly susceptible, and Negroes very slightly so. The other races appear to occupy intermediate positions. Age and sex and the corresponding differences in habits influence the amount of infection and also affect the injury done by a given number of worms, for females are more injured than males and children more than adults.

Occupation is often a determining factor, in so far as it leads to habits which render the acquisition of worms more likely. In most countries agriculture and mining are the main hookworm occupations, but in most places the infection is not strictly agricultural but merely rural. The raising of such crops as coffee, tea, sugar, cacao, and bananas is particularly conducive to hookworm in soil-pollution countries since these crops are grown in moist, warm climates under conditions affording an abundance of shade and suitable soil; cotton and grain raising are much less dangerous since these crops are grown in drier areas, and cotton in unfavorable soil. Raising of rice and jute, mainly on flooded ground, is not associated with heavy hookworm infections. In China and Japan, where night soil is used as fertilizer, hookworm infection is more strictly agricultural and varies greatly with the type of crop produced and the manner in which the night soil is used. Especially heavy infections occur in districts where mulberries and sweet potatoes are raised, since ideal conditions for hookworm propagation are afforded.

Defecation habits are also of great importance. In soil-pollution countries the greater part of the infections are acquired while standing on previously polluted ground during the act of defecation. The concentration of the defecation areas, the extent to which people mingle in common areas around villages, the type of places selected, etc., are all influential factors. Wherever simple soil pollution is modified by the use of standing places or primitive latrines that keep the feet off the polluted ground and bring about an unfavorable concentration of fecal material, hookworm infections are light.

The wearing of shoes also affords a high degree of protection; in southern United States and Queensland heavy hookworm infection is almost entirely limited to children who are less than 14 to 16 years of age, since after the age of 14 shoes are habitually worn. Even simple sandals or wooden soles without uppers, as worn in parts of India, are effective.

Expectoration habits also have an important effect; those individuals who habitually spit out phlegm collecting in the mouth get rid of many of the hookworms which invade the body. From Suez to Singapore the Orient is polka-dotted with the red expectorations of betel-nut chewers; this prevalence of chewing, and consequent expectoration, is probably an important factor in keeping hookworm infections at a relatively low level in Far Eastern countries. A notion was formerly prevalent in our southern states that tobacco chewing is conducive to health. There is no virtue in tobacco juice *per se*, but the constant spitting entailed would have a salubrious effect.

Effect of Diet. Diet is of profound importance. As we shall see, most of the injury done by hookworms is the result of blood loss, for the replacement of which large amounts of iron, protein, and vitamins are required in the diet. If these are present in adequate amounts the host soon develops a partial immunity which results both in resistance to reinfection and in inhibition of reproduction and ultimate loss of worms already harbored—the so-called self-cure which Stoll in 1929 demonstrated in a striking manner in *Haemonchus* infections in sheep and which has since been shown to be a common phenomenon among intestinal nematodes and trematodes (see p. 23). In other words, a good diet, as Foster and Cort demonstrated long ago (1932), does not permit serious damage from hookworm infection to occur except when there are overwhelming initial infections with the blood loss so great that *no* diet can compensate for it. A diet deficient in protein, plus loss of protein resulting from the bloodsucking of worms already present, permits no protein reserve for the production of new gamma globulin in the form of antibodies, so no immune response can develop, or if developed will break down. Provision of iron under such circumstances does little good, for protein as well as iron is necessary for manufacture of hemoglobin, and the iron alone does nothing towards development of immunity. As Cruz (1948) pointed out, hookworm disease is essentially associated with malnutrition. The severity of hookworm disease in a community is measured more by the adequacy of the diet than it is by the average number of hookworms harbored or the degree of exposure to infection.

Pathology. PREINTESTINAL PHASE. When human hookworms enter the skin they may cause "ground itch" or "water sore," characterized by itching and inflammation, and often development of pustular sores from secondary bacterial invasion. Ancylostomes less consistently cause these effects than necators.

Some "foreign" species of hookworms, particularly *Ancylostoma braziliense*, commonly fail to find their way below the germinative

layer of skin, thus failing to reach blood or lymph vessels. They then wander aimlessly just under the surface, sometimes for 3 months or more, causing tortuous channels—a condition known as “creeping eruption” (Fig. 126). The severity of the reaction is conditioned by previous sensitization and the allergic responsiveness of the victim. A similar effect is produced by the European dog hookworm, *Uncinaria stenocephala*, but it usually lasts only 2 to 4 weeks; and Mayhew has observed a still less extensive and less durable eruption from the larvae of the cattle hookworm, *Bunostomum phlebotomum*.



FIG. 126. Creeping eruption; *left*, typical lesions, including results of scratching an infected leg; *right*, lesions experimentally produced by application of a pure culture of *Ancylostoma braziliense* to the forearm. (From photographs by W. E. Dove.)

In highly allergic individuals *A. caninum* may cause severe skin reactions, though not typical creeping eruption. Creeping eruption is common on the coasts of southern United States and tropical America, where children play in sandpiles or adults on bathing beaches that are the chosen defecation sites of dogs and cats infected with *A. braziliense*. It could be prevented by excluding dogs and cats from such places, or bathers from beaches that are not washed by tides. Millspaugh and Sompayrac (1942) reported that in Florida creeping eruption incapacitated a considerable number of naval personnel. The most effective treatment is local freezing, shortly ahead of the end of the inflamed burrows, by application of ethyl chloride sprays or CO₂ snow. Control of dog and cat hookworms is considered on pp. 427–428.

The next effect of *human* hookworms is in the lungs, where the burrowing larvae may predispose to pulmonary infection or even cause

pneumonia symptoms themselves, if numerous. Rodents, in which hookworm larvae migrate to the lungs, die of extensive pulmonary hemorrhages if large doses are administered.

In repeatedly infected cases many larvae are frustrated in their migration through the body by the development of immunity. Immunized serum causes precipitates to form about the mouth, intestine, anus, and excretory pore of migrating larvae, probably directed against digestive enzymes or metabolic products of some kind. The larvae are also immobilized, and many are destroyed by encapsulation and phagocytosis in the skin, lymph glands, or lungs. The eosinophilia and occasional leucocytosis associated with hookworm infection probably result from liberation of proteins from such captured worms in partially immune persons. This larval phase of infection was emphasized by Ashford, Payne, and Payne (1933).

INTESTINAL PHASE. After several weeks, as the worms are maturing in the intestine, there may be some nausea, abdominal discomfort, and sometimes diarrhea, but the principal effects are due to anemia, resulting from the constant sucking of blood. Wells (1931) calculated that 500 *A. caninum* in a dog may suck nearly a pint of blood per day. The permanent loss of most of the iron, as well as large amounts of protein, causes reduction in number and size of corpuscles and in their hemoglobin content, unless *both* the iron and the protein are adequately replaced in the diet. In children the diversion of nutriment to keep the hemoglobin up to standard interferes with normal growth, thus causing a stunting in size.

When the repair cannot keep pace with the damage and immunity fails to develop, symptoms appear. In severe cases the hemoglobin may be reduced to 30 per cent or less, with 2,000,000 or less corpuscles per cu. mm. The most noticeable symptoms are a severe pallor; extreme languor and indisposition to play or work, popularly interpreted as laziness; a flabbiness and tenderness of the muscles; breathlessness after slight exertion; enlargement and palpitation of the heart, with weak and irregular pulse; edema, making the face puffy and the abdomen "pot-bellied"; a fish-like stare in the eyes; reduced perspiration; more or less irregular fever; and heartburn, flatulence, and abdominal discomfort. The appetite is capricious, and frequently there is an abnormal craving for coarse "scratchy" substances such as soil, chalk, and wood. Severe hookworm cases in our southern states a few decades ago were often "dirt-eaters," though they rarely admitted it.

Children may suffer several years' retardation in physical and mental development, with puberty long delayed. The mental retardation results in stupidity and backwardness in school, and there are

sometimes other nervous manifestations, such as dizziness, insomnia, optical illusions, general nervousness, and fidgety movements.

The effects of hookworm infection are particularly severe during pregnancy, when the demand for protein and iron by the developing fetus puts an extra drain on the mother. Hookworm is the cause of a tremendous number of stillbirths and is believed by some to be a more serious complication of pregnancy than even syphilis or eclampsia. The reduction of labor efficiency from hookworm infection may amount to 25 or even 50 per cent, and there may be additional loss from sickness and death.



FIG. 127. Hookworms on wall of intestine, showing lesions. (After International Health Board, chart.)

Grades of Infection. In earlier days much emphasis was put on the mere presence or absence of infection. Darling in 1918 was the first to emphasize the importance of the *number* of hookworms harbored, though now we know that even the number may not mean much without considering the adequacy of the diet as well. The first efforts to estimate the number of hookworms harbored were based on worm counts after treatment, but the technical difficulties were too great. In 1923 Stoll devised an easy method of counting the eggs per gram in the feces of infected people and demonstrated that there was a rough correlation between eggs per gram (e.p.g.) and number of worms harbored. This method, or modifications of it, has been a valuable yardstick not only for measuring the hookworm burden of communities and the efficacy of control measures, but also for demonstrating the effect of different degrees of infection under varying conditions.

Slight infections with 50 worms or less are practically harmless except

in a person who needs additional food much more than he needs hookworm treatment; ordinarily such infections can safely be ignored. Even several hundred worms may produce no measurable symptoms in a person on a good diet, not pregnant, and not suffering from overwork or chronic disease, but Hill and Andrews (1942) in Georgia found a falling off in hemoglobin in the group with 2000 to 4000 eggs per gram (about 60 to 120 worms), which became marked in the 4000 to 8000 group and severe in cases with over 15,000 e.p.g. It is not possible to set any definite limits to these grades of injury in the case of any individual, but in communities the percentage falling into different egg-count groups gives a useful index to the hookworm burden, and correlation with hemoglobin percentages gives valuable information on susceptibility to injury under existing dietary and environmental conditions.

The erroneousness of judging hookworm infection by the percentage of people infected is nowhere better demonstrated than in Bengal, where an average of at least 80 per cent of the 46,000,000 inhabitants are infected, a condition which some years ago was spoken of as "staggering." But egg counts show that in 90 per cent of the area of Bengal the average number of worms harbored per person is less than 20, and not more than 1 per cent of the people are estimated to have over 160 worms and almost none over 400. In other words, instead of being a staggering problem involving the health of over 35,000,000 people, it is negligible from the public-health point of view.

Diagnosis. Hookworm infection can rarely be diagnosed with certainty by symptoms, but a positive diagnosis is easily obtainable by modern flotation methods of finding eggs in the stools. If it is only desired to find infections which need treatment, the simple smear method suffices, but more accurate diagnosis can be made by the methods discussed on p. 255. Community diagnosis, i.e., the hookworm burden of a community, can be ascertained by means of egg counts as described on p. 256.

The collection of fecal samples for diagnosis on a large scale can be made in bottles containing a few cubic centimeters of antiformin as described by Maplestone in 1929, or with 1 per cent NaCl added in the proportion of 30 : 1 as suggested by Maplestone and Mukerji in 1943. In either case the specimens can be sent to a central laboratory for examination, thus eliminating the necessity for a moving field laboratory, for the specimens are useful for both diagnosis and egg counts even after several days.

Treatment. The treatment of hookworm infection has undergone an interesting evolution. Thymol, introduced in 1880, was the classi-

cal treatment for many years but was superseded by oil of chenopodium during World War I. The latter drug is more effective against *Ascaris* than against hookworms, and is often combined with tetrachlorethylene when both worms are present. It has the advantage of cheapness and of being administered in liquid, but it is too toxic for general use. In 1921 carbon tetrachloride, previously best known as a fire extinguisher, was introduced and within a few years became widely used all over the world; now, however, it is seldom used because of the damage it does to the liver, and its dangerousness when there is a calcium deficiency.

In 1925 tetrachlorethylene, and in 1930 hexylresorcinol, were found to be highly effective and relatively non-toxic, and these two drugs are the ones most frequently used at present. Tetrachlorethylene is given in soft gelatin capsules in a dose of 0.5 to 0.6 cc. per lb. of body weight, up to a maximum of 4 or 5 cc. This removes about 75 per cent of the necators, with complete cures in about two thirds of the cases, but it is considerably less effective, as are other drugs, against ancylostomes. The only side effects are a brief burning sensation in the stomach, slight nausea, and a drunken sensation. Best results are obtained if the patients are treated before eating in the morning and *not* given a subsequent purge (Carr et al., 1954).

Hexylresorcinol in crystalline form in capsules (crystoids) eliminates about 60 to 75 per cent of the worms harbored and has the added advantage of eliminating 90 to 100 per cent of *Ascaris* and 50 per cent of *Trichuris*. The dose for adults is five 0.2-gram pills (1 gram), three to four for a school child, and one for each 2 years of age up to 6; a sodium sulfate purge is given 2 hours later. This less toxic drug is preferable in pregnancy and illness, and for delicate children. Both tetrachlorethylene and hexylresorcinol have the disadvantage of having to be administered in capsules.

In places where *Ascaris* infections are common a good plan is to give hexylresorcinol first to eliminate the *Ascaris* and most of the hookworms, following it a week or 10 days later with a treatment of tetrachlorethylene. The latter drug irritates but does not kill *Ascaris*, and sometimes causes them to tangle themselves in knots that block the intestine and must be removed by operation.

Another drug that has shown promise in dogs is *n*-butyl chloride, which is effective against *Ascaris* and whipworms also, but has not yet come into general use for human infections.

Improvement after deworming is very slow, whereas administration of iron in the form of ferrous sulfate or gluconate at the rate of 1 gram per day for adults, with a rich diet in protein and vitamins, causes

rapid improvement. In weak, anemic cases, and in pregnancy, the blood should be built up by iron and protein therapy before an anthelmintic is given.

Mass Treatment. Mass treatment, first advocated by Darling, greatly speeds up hookworm campaigns. By this is meant the treatment, without preliminary diagnosis, of an entire community at one time, when the great majority of the individuals are found to be infected. The diagnosis itself does not require so much time, but the difficulty in obtaining fecal samples from primitive people is well known to anyone who has tried it; in many cases it is quite impossible. If all the members of a community are treated at once, preferably in a dry or cold season when rapid reinfection from an already badly infested soil cannot occur, the reduction in infection is striking and durable. In Fiji practically the entire population was treated in two years, a feat which could not have been accomplished in *any* length of time by the older methods, for, long before even a fair percentage of the people could have been covered by diagnostic measures, those first treated would again have been infected from their untreated neighbors. The original mass treatment in Fiji was made in 1922 and 1923 and was followed by improvement in the sanitary conditions of the soil. In 1935 Lambert reported that clinical hookworm disease was still rare in Fiji; the people were healthier, happier, and more prosperous, and hookworm had been eliminated as an important economic factor.

Prevention. Theoretically, few if any diseases can be as simply, as certainly, and as easily controlled as hookworm. Diagnosis is easy and accurate, treatment reduces existing infections to a negligible point, and reinfection can be prevented by stopping soil pollution, for no other animals, except possibly pigs and apes, and these only in some localities, harbor human hookworms. But in the prevention of soil pollution the sanitarian runs into a snag. The difficulties involved in this seemingly simple procedure are infinitely greater than the average inhabitant of a civilized sanitary country would suspect. It involves an attempt to induce hundreds of millions of people in tropical and sub-tropical countries to abandon habits which have been ingrained in them for countless generations and in some instances dictated by religion, and to adopt in their place unfamiliar habits that seem to them obnoxious and undesirable and the reasons for which they cannot readily grasp.

Even in our own southern states a survey in the early part of the present century showed that in the hookworm belt about 68 per cent of the rural homes were not provided with privies of any kind. Fortunately there has been much improvement in this respect, but in many

rural districts where privies do exist, their use is restricted to the women and children or to the family of the manager. Among the "jibaros" or plantation laborers of Puerto Rico, of 61 hookworm patients who were questioned, 55 never had used privies of any kind, and of the 6 who did occasionally use them, only 2 lived in rural districts.

Five weapons are available for use in the control of hookworm: treatment, dietary supplements, protection of the feet, disinfection of feces or soil, and prevention of soil pollution. Mass treatment gives immediate relief and slows up the rate of reinfection on account of the great reduction in number of eggs reaching the soil; but treatment alone, unless consistently repeated, is inadequate, since it has never yet been and probably never will be found feasible to eliminate all the worms, and reinfection inevitably follows. In Puerto Rico, Hill in 1927 treated 1000 people in an isolated valley and eliminated 97.5 per cent of the worms. In one year the residual infection increased to 500 per cent and was nearly 20 per cent of the infection before treatment.

Cruz and de Mello (1945), recognizing the extent to which hookworm disease is influenced by diet, suggested the wholesale addition of iron to food as a preventive measure, just as iodine is added to water to prevent goiter. It is more difficult, since the iron used must be in a cheap, stable form and must not markedly discolor food or give objectionable tastes. In Brazil they suggested ferrous sulfate added to cassava meal, or iron and ammonium citrate to beans. For people with hookworm anemia they recommended 1 gram per day until the hemoglobin is normal, then 0.5 gram for 80 days, and then 0.25 gram for 80 days more. Provided that there is adequate protein in the diet, such a program not only would eliminate symptoms but also would permit development of immunity, reduce the number of eggs reaching the soil, and eventually lead to a much lower hookworm burden even without improvement in sanitary conditions.

Wearing of footgear is a valuable measure when it can be consistently enforced; it is essential for individuals in infected areas who desire to protect themselves. However, the wearing of footgear is often as difficult to enforce in the tropics as is sanitary disposal of feces, and it is far less effective in ultimate control. It is a valuable temporary measure, comparable with the use of mosquito screens for the control of malaria, but it does not get at the root of the trouble.

Disinfection of soil or feces is difficult. Salt can be effectively used under certain conditions, especially in mines, and lime added to feces is an effective method of killing hookworms in night soil. Sodium borate, calcium cyanamide, and urea, especially the first, have been found fairly promising in eliminating hookworm larvae from limited

areas, e.g., in dog or cat yards. Methyl bromide applied to the ground under an airtight covering of glue-coated paper (1 lb. to 64 sq. ft.) kills all worm larvae and eggs, and protozoan cysts as well, but it is too expensive except for small areas, for valuable breeding stock, zoos, etc. Further experiments are desirable in adding small amounts of such substances as sodium borate and phenothiazine to the diet of animals. Low-level doses of phenothiazine (2 grams daily to horses) reduces the number of strongylid eggs passed, and affects their fertility.

Prevention of soil pollution, then, remains as the only dependable method of control of human hookworms under most conditions. The efforts of sanitarians in this direction are not so prone to be too little and too late as to be too much and too soon; we are likely to try to force on tropical natives our own ideas of sanitary arrangements, just as we try to force on them our ideas of ethics, religion, clothing, and food habits. It is better as a beginning to teach the coolie to defecate into a trench, from a log over a ditch, or from a low branch or root of a tree or even from a projecting stone, than to build an enclosed fly-proof latrine, which he promptly befouls and which prejudices him against latrines in general. Meanwhile education will gradually alter prejudices, and eventually really sanitary privies to control such diseases as dysentery and typhoid as well as hookworm will be possible.

In the United States Andrews (1942), in Georgia, pointed out that hookworm work should be directed toward the detection, prevention, and control of clinical infections. Most of these could be found by examination of large, low-income white families living on sandy or sandy-loam soil, without sanitary conveniences, and showing evidence of anemia. Attention should, he thinks, be concentrated on these families, omitting work where there is good sanitation, clay soil, good income, or a Negro population. The bulk of hookworm morbidity would then be revealed at a minimum of time and expense.

The campaign against hookworm disease, which has been sponsored especially by the International Health Board, although a most worthy end in itself, leads to even greater benefits, for the work, while bringing relief to hundreds of thousands of suffering people, is at the same time serving the more useful purpose of creating a popular sentiment in support of permanent agencies for the promotion of public health. In the United States it led to rapid advances in rural hygiene and the establishment of county health organizations all over the country, and similar local organizations have been brought to life in many other countries. Schools of hygiene have been established in various parts of the world to provide trained men to carry on the work. The ultimate results which may come from the simple beginnings centered on the

eradication of hookworm disease are impossible to estimate, but in the light of the tremendous accomplishments which we have seen realized since the inception of the work of the International Health Board about 1910 the outlook for the future is bright indeed.

Other Strongylata

Other Hookworms. *Ancylostoma caninum*, *A. ceylanicum*, and *A. braziliense*, important parasites of dogs and cats, were discussed on pp. 411 and 413. In Europe dogs commonly harbor *Uncinaria stenocephala*, a hookworm related to *Necator* but with only one pair of lancets in the depth of the mouth capsule. The hookworms of cattle, sheep, and other ruminants belong to the genus *Bunostomum*, also related to *Necator* but with the dorsal lobe of the bursa asymmetrical.

Family Strongylidae. The members of this family have globular, golbet-shaped or cylindrical deep or shallow mouth capsules, with a crown of leaflets (corona radiata) guarding its entrance (Fig. 128). The family contains a number of species which are injurious to domestic animals and a few which are more or less frequent parasites of man. Among the more important forms are species of *Oesophagostomum* in pigs, ruminants, and primates; *Strongylus* and members of the subfamily Cyathostominae (also called Trichoneminae or Cylicostominae) in horses; *Chabertia* in sheep and goats; and *Stephanurus* (kidney worm) in pigs.

The esophagostomes of pigs and ruminants and the strongyles of horses, as well as many of the trichostrongylids (discussed on pp. 433 to 435), are very susceptible to treatment with phenothiazine, but this drug is relatively ineffective for worms of the hookworm type.

All the members of the Strongylidae have a life cycle similar to that of the hookworms except that the infective larvae of most genera do not penetrate the skin but are ingested with vegetation. The larvae have long pointed tails and are protected from desiccation by their sheaths. They are frequently found in an apparently dry state, but viable, curled up on the under side of grass or leaves. Many species retreat to the upper layers of the soil during the heat of the day. They are susceptible to excessive heat or direct sunlight but not to freezing. Some of the species, e.g., *Strongylus* spp. (Fig. 128A), go on a roundabout tour through the body before growing to maturity in the intestine, but most of them spend their apprenticeship in nodules in the walls of the gut.

The Cyathostominae or "small strongyles" (Fig. 128B) of horses also pass the first part of their parasitic life as larvae in nodules in the walls of the large intestine and cecum, but the nodules are smaller.

One species of *Strongylus* (*S. vulgaris*) frequently causes aneurisms of the mesenteric arteries in horses and is a cause of colic; the larvae migrate through the intestinal wall and between the layers of the mesentery, enter the mesenteric artery where they develop in blood clots, and finally migrate back to the colon wall and into the lumen of the intestine.

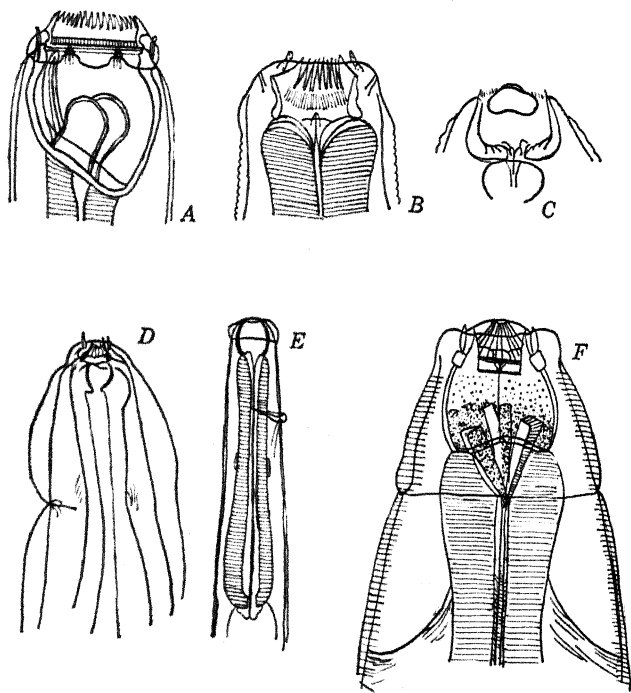


FIG. 128. Heads of various types of Strongylata. A, *Strongylus vulgaris*; B, *Trichonema tetracanthum*; C, *Stephanurus dentatus*; D, *Oesophagostomum bifurcum*; E, fourth-stage larva of *Oesophagostomum*; F, *Ternidens deminutus*. (A, B, C, and F after Yorke and Mapleston, *Nematode Parasites of Vertebrates*, 1926. D after Travassos and Vogelsang, *Mem. Inst. Oswaldo Cruz*, 1932; E after Monnig, *Veterinary Helminthology and Entomology*, 1949.)

The esophagostomes or nodular worms are common and injurious parasites of pigs, sheep, goats, cattle, apes, and monkeys, and are occasional parasites of man. They are about the size of hookworms but have a shallow mouth capsule with a corona, and a groove behind the head on the ventral side (Fig. 128D). When the infective larvae are eaten and liberated from their sheaths they do not at once establish themselves in the lumen of the intestine but first burrow into the lining

of the large intestine where the host forms a tumor-like nodule around them (Fig. 129).

In young non-immune animals the worms return to the lumen of the intestine in 5 to 8 days and grow to maturity, but, as immunity develops, the tissue reaction becomes greater and many of the worms remain imprisoned in the nodules, even for months. Older animals may have the large intestine covered with nodules but have very few

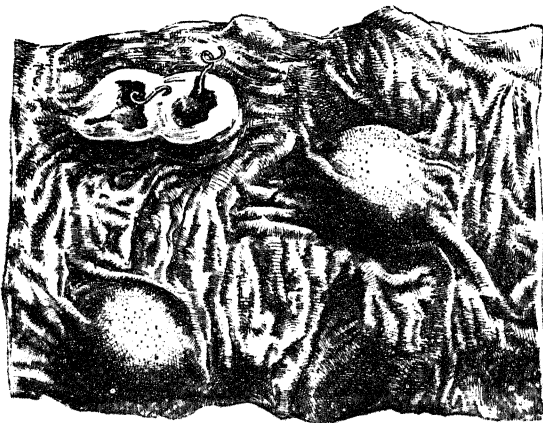


FIG. 129. Tumors or nodules of *Oesophagostomum bifurcum* in large intestine of an African. $\frac{3}{4}$ natural size. (After Brumpt, *Précis de parasitologie*, 1949.)

adult worms. The nodules are $\frac{1}{2}$ to 1 in. in diameter and contain a greenish pus-like substance surrounding the immature worm. Progressive weakness and loss of weight are characteristic, with diarrhea in earlier stages.

Several species of these worms, normally inhabiting apes and monkeys, have been found on rare occasions in man, but, since the eggs are indistinguishable from those of hookworms, human cases may be much commoner than is suspected.

In ruminants and apes the infection commonly produces severe emaciation and prolonged dysentery, and sometimes fatal peritonitis. In the encysted stage the worms are unaffected by anthelmintics, and they are difficult to dislodge even when free on account of their location in the large intestine.

A related worm, *Ternidens deminutus*, is a common parasite in natives of parts of southern East Africa; Sandground (1931) found light infections in 50 to 65 per cent of natives examined in two villages in southern Rhodesia. The eggs measure about 84μ by 51μ , and are usually in the eight-celled stage when passed. In various monkeys this

parasite occurs all the way from the Atlantic coast of Africa to south-east Asia and Celebes. The worms, which are bloodsuckers, superficially resemble hookworms but have a deep goblet-shaped buccal capsule with three teeth in the depths (Fig. 128E). Its eggs may easily be mistaken for those of hookworms, but unlike hookworms *Ternidens* forms nodules in the intestine and is not expelled by the usual hookworm remedies, so it may be much commoner in countries inhabited by its reservoir hosts than the records indicate.

A strongylid which causes much damage in the colon of sheep is *Chabertia ovina*, a rather large worm, the females measuring up to 20 mm. long, and having a globular mouth capsule with no teeth but with two crowns of extremely fine leaflets. It is a northern parasite; its larvae are capable of development at very low temperatures. In sheep it is 9 to 10 weeks after infection before eggs appear.

Stephanurus dentatus, the kidney worm of pigs, has a globular capsule with a very feeble corona (Fig. 128C) and a poorly developed bursa that is subterminal. After developing to the infective stage outside the body the larvae enter the body either by mouth or through the skin and go by way of the bloodstream to the liver, where they live and grow for a few months, eventually making their way to the kidneys. Here they become embedded, the eggs reaching the ureters and being excreted with the urine. It is rather injurious to pigs, and entails considerable economic loss from condemned liver and kidneys.

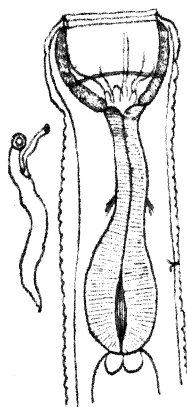


FIG. 130. Right, head of ♀ *Syngamus kingi* (after Leiper, *J. Soc. Trop. Med. Hyg.*, 1913). Left, a pair of worms in copula.

Family Syngamidae. This family (see p. 409) includes bloodsucking worms that live in the trachea and bronchi of birds and mammals. The worms are called gapeworms or forked worms because the male remains permanently attached to the vulva of the female by its bursa, giving a forked appearance (Fig. 130); the females are 15 to 20 mm. long and red in color. The eggs measure about 85 by 50 μ and are in early stages of segmentation when oviposited. From the air passages they are coughed up and swallowed, passing out with the feces. Although direct infection with embryonated eggs is possible, the eggs

are frequently eaten by various invertebrates, in which the embryos hatch and become encapsulated, the invertebrates thus becoming "transport" hosts. Earthworms are particularly important hosts and may harbor the infection for years, but slugs, springtails, maggots, and others are

also involved. When swallowed, the infective larvae penetrate the mucous membranes and are carried to the lungs by the blood stream.

One species, *Syngamus trachea*, is an injurious parasite of turkeys, young chickens, and pheasants, and a related worm affects geese. Many passerine birds such as robins, blackbirds, crows, and starlings also harbor gapeworms; although Goble and Kutz in 1945 showed that several species are involved, these birds can serve as carriers of the poultry parasite. A number of instances of human infection with gapeworms have been recorded, all but one of them in tropical America;

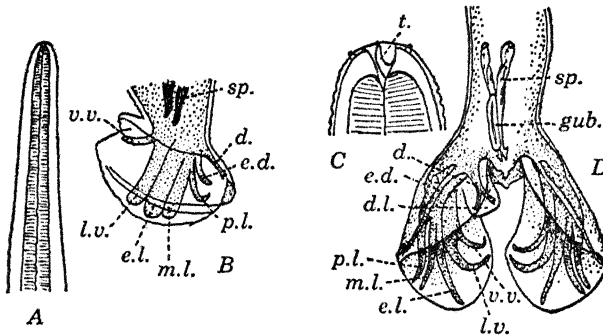


FIG. 131. *A* and *B*, head and bursa of *Trichostrongylus colubriformis*; *C* and *D*, head (greatly enlarged) and bursa of *Haemonchus contortus*; *t.*, buccal tooth; *d.l.*, dorsal lobe; *gub.*, gubernaculum; other abbreviations as in Fig. 120. (*B*, after Looss; *C*, after Yorke and Maplestone, *Nematode Parasites of Vertebrates*, 1926; *D*, after Ransom.)

in most of these cases the species concerned was *S. laryngeus* of cattle. The worms attack the pharynx, trachea, or neighboring air spaces in the head or throat, often causing nodules at the point of attachment. Coughing and gaping are the usual symptoms, and chicks may die from obstruction of the trachea. Immunity develops quickly, but chicks lose their worms much more rapidly than turkeys. Barium antimonyl tartrate, inhaled as a dust, is recommended for treatment. Addition of 4 per cent phenothiazine to the mash of chickens controls the infection, but it only kills the young worms when they hatch in the intestine, so it must be used continuously.

Family Trichostrongylidae. These worms, recognizable by the finely drawn-out head without a large buccal capsule, together with a well-developed bursa in the male (Fig. 131), are very important parasites of domestic animals. Sheep, goats, and cattle suffer severely from the stomach worm, *Haemonchus contortus*, and to a less extent from species of *Trichostrongylus*, *Cooperia*, *Nematodirus*, and *Oster-*

tagia. *Trichostrongylus axei* also lives in the stomach of horses. Pigs are infected with *Hyoststrongylus*. These genera have the following characters:

1. *Haemonchus*: length, ♀ 20–30 mm., ♂ 10–20 mm.; small buccal cavity with a lancet; ♀ with conspicuous vulvar flap; ♂ with short, stout spicules and small asymmetrical dorsal lobe on bursa. (Fig. 131C, D).

2. *Ostertagia*: length, ♀ 8–9 mm., ♂ 6–8 mm.; head with very small buccal cavity; ♂ with short spicules and small accessory bursal membrane dorsally.

3. *Cooperia*: length, ♀ about 6–7 mm., ♂ about 5–6 mm.; head 25 μ in diameter; no cervical or prebursal papillae; ♂ with short spicules, branches of dorsal ray lyre-shaped.

4. *Nematodirus*: length, ♀ 15–20 mm., ♂ 10–15 mm.; extremely slender; ♀ tail truncated with spine-like process; ♂ with filiform spicules, dorsal ray split to base.

5. *Trichostrongylus*: length, ♀ 5–6 mm., ♂ 4–6 mm.; head 10 μ in diameter; ♂ with short spicules, dorsal ray split only near tip. (Fig. 131A, B).

6. *Hyoststrongylus*: length, ♀ 5–8 mm., ♂ 4–5 mm.; very similar to *Trichostrongylus* but found only in pigs.

The life cycles of all these worms are essentially the same; the eggs develop outside the host's body into long-tailed, sheathed larvae most of which are capable of withstanding considerable desiccation and live for a long time. They gain access to their hosts by being ingested with vegetation. They grow to maturity directly in the intestine, although some species burrow into the mucous membrane before becoming established in the lumen of the intestine, and some, e.g., *Ostertagia* and *Cooperia*, like esophagostomes, become enclosed in nodules in partly immune animals.

All these worms may cause a condition known as "verminous gastroenteritis" by veterinarians, but more often as "black rush," "black scours," etc., by sheep men. As with hookworms, severe infection is the result of poor nutrition or of overwhelming initial infections, for otherwise the animals soon build up an immunity resulting in "self-cure" by expulsion of the worms and resistance to reinfection. The occurrence of diarrhea, emaciation, failure to gain weight, anemia, poor wool production, and general weakness and unthriftiness in the presence of considerable numbers of trichostrongylids is *prima facie* evidence of faulty nutrition, resulting either from poor pasturage or, in nursing animals, from inability to get adequate milk from the mothers. *Haemonchus contortus* is the only important bloodsucker in this group, and in heavy infections in young animals may cause enough blood loss to produce severe anemia before immunity can develop, and thus be a primary pathogen, whereas the others are all secondary to malnutrition as Whitlock (1949, 1951) pointed out. Phenothiazine treatment is

indicated in *Haemonchus* infections that are producing anemia, but is of much less importance than improved nutrition under other conditions.

Haemonchus contortus (stomachworm or wireworm) (Fig. 131C, D) lives in the stomach (abomasum) of sheep, goats, and cattle, and may play havoc with young animals. It is much larger than other trichostrongylids, the females being about 1 in. long and the males about $\frac{1}{2}$ in. It has a world-wide distribution. One human case has been reported from Brazil.

Ostertagia are also stomach parasites; they are brownish hair-like worms less than $\frac{1}{2}$ in. long. *O. ostertagi* is commoner than *Haemonchus* in cattle in western United States.

Trichostrongylus (Fig. 131A, B) contains many species of minute reddish hairworms only about $\frac{1}{4}$ in. in length. *T. axei* lives in the stomach of ruminants and horses, and rarely in man. Sheep and goats suffer from a number of species, *T. colubriformis*, *vitrinus*, and *capricola* being the commonest. Andrews (1939) showed that in pure experimental infections *Trichostrongylus* produces a profuse, continuous diarrhea. Animals with very heavy infections die after several weeks.

Human *Trichostrongylus* infections are fairly common in parts of the Middle East, Far East, and the tropics, with incidences running as high as 80 per cent in some localities, e.g., in parts of Japan. In Egypt and other places a high incidence of *Trichostrongylus* infections probably reflects the close association of man and animals, especially where they share the same house. Since the infections are usually very light they are of little consequence, but the eggs resemble those of hookworms enough to be mistaken for them by people unfamiliar with them; they are, however, larger, more slender, and more pointed at one end. The worms are not expelled by hookworm remedies. For the most part the species involved have not been determined.

Nematodirus and *Cooperia* also contain species parasitic in the duodenum of sheep and goats, and the latter also in cattle. *Nematodirus* is remarkable for its large eggs, up to 200 μ or more long, and for its larvae, which undergo two molts in the egg before they hatch and climb to a vantage point on grass. *Hyostromylus*, the red stomachworm of pigs, is only $\frac{1}{8}$ in. long and red in color. In poorly nourished pigs it produces effects similar to those of most other trichostrongyles.

Mention should also be made of the subfamily Heligmosominae, which are parasites of rodents; they are tiny red worms which have a single ovary and uterus and which roll their bodies in spirals.

Metastrongylidae (Lungworms). These slender worms inhabit various parts of the respiratory system of mammals; most of them

inhabit the fine branches of the bronchial tubes of the lungs, but one species lives in the heart and pulmonary arteries of dogs, and others in the frontal sinuses of tigers, skunks, and mink.

Species of the genus *Dictyocaulus*, which inhabit the bronchial tubes of sheep, cattle, and horses, are thread-like worms several inches in length. In a number of ways they show affinity with trichostrongylids; they have short, robust spicules, a vulva near the middle of the body,

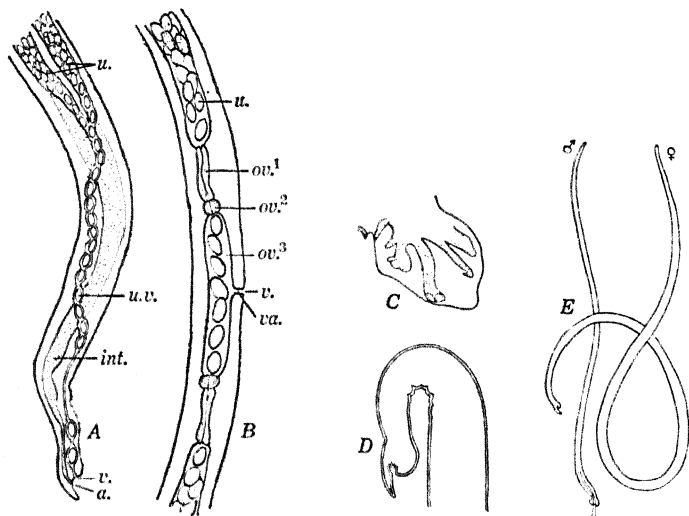


FIG. 132. *A* and *B*, comparison of female reproductive system of a metastrongylid (*A*) and a trichostrongylid (*B*); *a.*, anus; *int.*, intestine; *ov.¹*, ejector of ovejector; *ov.²*, sphincter of ovejector; *ov.³*, chamber of ovejector; *u.*, uterus; *u.v.*, uterine vagina; *v.*, vulva; *va.*, vagina. *C*, *D*, and *E*, *Metastrongylus elongatus*; *C*, bursa of male; *D*, posterior end of female; *E*, male and female worms. $\times 3$. (Adapted from various authors.)

well-developed ovejectors, and no intermediate hosts. The larvae hatch in the bronchi of the host and are either coughed out or swallowed and passed in the feces. They are peculiar in not feeding at all in the free-living phase; they molt twice, and both shed cuticles are retained for a time. They infect by being swallowed, and they reach the lungs via the lymph system. These worms may cause coughing and bronchitis, and in sheep may block off so much of the lungs as to be fatal.

Lungworms of the subfamily Metastrongylinae have medium or very long spicules, and the vulva is a short distance in front of the anus (Fig. 132*A*). In the genera *Metastrongylus* and *Choerostongylus*, important parasites of pigs, the spicules are very long and the female has a finger-like tail (Fig. 132*D*). These pig parasites produce thick-shelled

embryonated eggs which hatch when ingested by certain species of earthworms, in which they develop to the infective stage. Members of the subfamily Protostrongylinae (*Protostrongylus* and *Muellerius* of ruminants, *Aelurostrongylus* of cats, and several genera in deer) develop in mollusks. The embryos hatch before leaving the body and burrow into the foot of various land snails and slugs, where they undergo two molts, become encapsulated, and remain infective as long as the snail remains alive. As Hobmaier remarked, the utilization of mollusks as intermediate hosts by these worms probably grew out of their habit of seeking protection from desiccation in the slime of the mollusks.

Only one species of lungworm, *Metastrongylus elongatus* (Fig. 132) of pigs, has been found in man, and this only three times.

Attempts at treatment of lungworms in animals have been made by tracheal injection of various substances and by inhalation of chloroform or fumes of tar, sulfur, etc., but with good care the animals resist the infection and soon lose their worms.

Of very great interest for helminthology in general is the demonstration by Shope (1939) that swine influenza is caused by a combination of certain influenza bacteria and a virus, and that the virus is harbored by the larvae of lungworms (*Metastrongylus*), which serve as vectors for it. The virus survives as long as three years in lungworms encapsulated in earthworms; it is thus perpetuated from one outbreak to another. Species of *Strongylus* have likewise been found to harbor the virus of swamp fever of horses, and *Trichinella* has been shown to act as a vector for the virus of lymphocytic choriomeningitis. The fluke *Nanophyetus salmincola* is a carrier of the rickettsia of salmon-poisoning, and *Heterakis* (p. 448) for the flagellate, *Histomonas* (p. 127). The role of helminths as vectors for viruses and other disease agents is, however, still an almost virgin field.

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HOOKWORMS

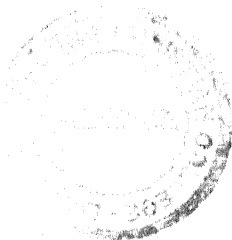
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OTHER STRONGYLATA

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Other Intestinal Nematodes

ASCARIDATA. I. ASCARIDOIDEA

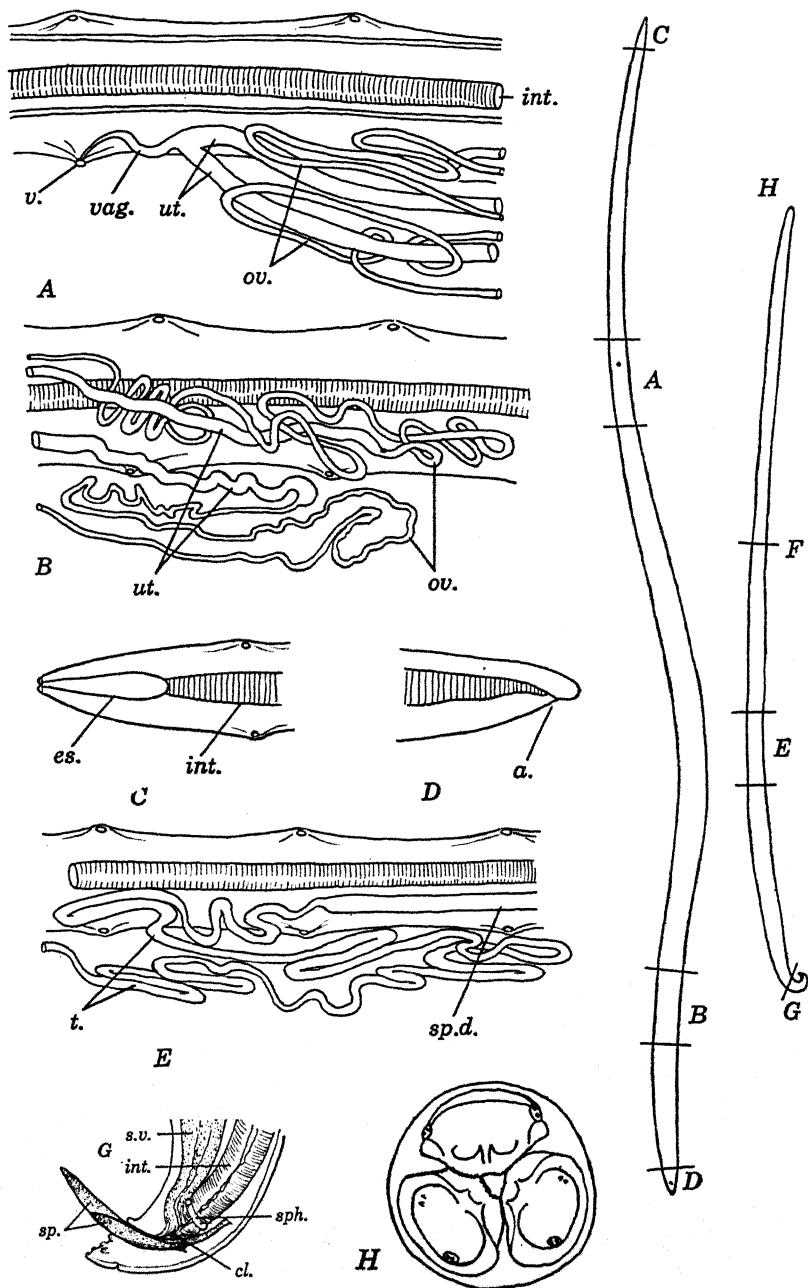
As noted on p. 390, the suborder Ascaridata consists of two superfamilies, the Ascaridoidea and the Oxyuroidea. The former contains for the most part relatively large, opaque, *Ascaris*-like worms of which there are numerous species parasitic in all kinds of vertebrates, whereas the latter contains smaller, transparent, *Oxyuris*-like worms which are parasitic mostly in the cecum and colon of vertebrates and also of insects.

Ascaris lumbricoides

General Account. *Ascaris lumbricoides* has undoubtedly been one of man's most faithful and constant companions from time immemorial, probably since he began domesticating pigs and by his habits made possible the development of a special strain particularly adapted for residence in his own intestine. This worm has clung to mankind successfully through the stone, copper, and iron ages, but plumbing threatens eventually to dissolve the partnership if children can be "yard-broken" early enough. Wherever soil pollution prevails, if only by toddlers in the dooryards, and wherever there is warmth and moisture, *Ascaris* infections are common.

Although *Ascaris* is one of the longest-known human parasites, it is a remarkable fact that important details of its life cycle were unknown before 1916, and the factors influencing its epidemiology were not elucidated until after 1930. One reason for this is that *Ascaris* infec-

FIG. 133. *Ascaris lumbricoides*. Entire worms at right, 1/2 natural size. At left, dissected parts corresponding to letters on whole worms. A, region of vulva of ♀; B, region where uteri change to ovaries; C, anterior end; D, posterior end of ♀; E, region where sperm duct changes to testis; F, region where coils of testis end anteriorly (no dissection of this shown); G, posterior end of ♂; H, anterior view of lips. Abbreviations: a., anus; cl., cloaca; es., esophagus; int., intestine; ov., ovary; sp.d., sperm duct; sp., spicules; sph., sphincter; s.v., seminal vesicle; t., testis; ut., uterus; v., vulva; vag., vagina.



tions have in general not been taken very seriously and their injurious effects have been minimized, whereas the effects of hookworm have often been exaggerated. Early in the present century *Ascaris* came into the limelight as an injurious and sometimes dangerous parasite. When a parasite steps into prominence nowadays it has little more chance to keep any details of its life and habits under cover than has a candidate for public office.

Morphology. *Ascaris lumbricoides* is a large nematode; the females commonly reach a length of 8 to 14 in. or even more, and are 4 to 6 mm. in diameter. The males are 6 to 12 in. long but distinctly more slender than the adult females; they are always distinguishable by the curled tail, whereas the females have a blunt tail (Fig. 133). Both sexes are more slender at the head end.

In common with other members of the Ascaridoidea, *A. lumbricoides* has the mouth guarded by three lips, one dorsal and two latero-ventral, each with minute papillae (Fig. 133H). The esophagus is nearly cylindrical and is followed by a flattened, ribbon-like intestine. The vulva is situated about one-third the distance from head to tail. The coiled tail of the male is short and provided with a characteristic number and arrangement of papillae but no alae. This worm is a favorite object for the study of nematode anatomy, since it is always easily obtainable and is easily dissected. An *Ascaris* morphologically indistinguishable from the human species is a very common parasite of pigs, but the two worms are physiologically distinct; eggs from one host species do not readily infect the other, so pigs are negligible as reservoirs. Both pigs and dogs may, however, be important in the dissemination of eggs which they have ingested with human feces.

Life Cycle. The adult *Ascaris* normally lives in the small intestine, where it is supposed to feed on the semidigested food of the host, but there is evidence that it commonly bites the mucous membranes with its lips and sucks blood and tissue juices to some extent. Reid (1945) showed that a related worm, *Ascaridia galli* of chickens, is highly susceptible to host starvation for 48 hours, just as are tapeworms, and that many are expelled when their stored glycogen supply is depleted.

The egg production of *Ascaris* is astounding. Cram (1925) estimated the number of eggs contained in a mature female worm to be as high as 27,000,000, and the eggs per gram of feces for each female worm may be in excess of 2000. This would indicate a daily production of something like 200,000 eggs! Evidently the chances against the offspring of an *Ascaris* reaching a comfortable maternity ward in a human intestine are many millions to one.

The eggs (Fig. 57U, V) have a thick, clear, inner shell covered over

by a warty, albuminous coat which is stained yellow or brown in the intestine; they usually measure about 60 to 70 μ by 40 to 50 μ . Unfertilized eggs (Fig. 57W) are more difficult for a beginner to identify, since they are more elongate and less regularly oval in shape and have amorphous contents instead of the well-defined round cell of the fertilized eggs. The warty, albuminous coat dissolves off in sodium hydroxide, so in feces examined by Stoll's egg-count method the eggs may have only the thick inner shell.

The eggs are unsegmented when they leave the host. In order to develop they require a temperature lower than that of the human body, at least a trace of moisture, and oxygen. They are very resistant to chemical substances and will develop readily in weak formalin solutions or in sea water, but they can be killed by methyl bromide (see p. 428). They gradually degenerate at temperatures above 100°F. and cease development below about 60°F.; about 85°F. is the most favorable temperature. Complete drying is lethal, but in moist soil they remain viable for years. An enterprising German researcher seeded a plot of soil with *Ascaris* eggs; two persons ate unwashed strawberries raised on the plot each year for 6 years, and each year acquired a few *Ascaris*.

Under favorable conditions of temperature, moisture, and air the eggs develop active embryos within them in 10 to 14 days, but the embryos are not infective until they have molted inside the egg, becoming second-stage larvae; this requires an extra week.

When the eggs are swallowed the larvae hatch in the small intestine. They penetrate the mucous membranes and go on a sort of homeseeker's trip through the body, being carried by the blood stream to the liver, then the heart, and then the lungs. Here they burrow out and make their way through the trachea, throat, and esophagus back to the intestine, meanwhile having benefited from the trip by a growth from 200 to 300 μ to about ten times this length. The migration through the lungs takes place readily in rats, mice, guinea pigs, and other rodents as well as in the natural hosts, but after the return to the intestine the worms pass right on through in unnatural hosts and are voided in the feces.

The larvae of ascarids of pigs and horses perform the same migration through the liver and lungs and back to the intestine as does the human *Ascaris*, but work by Sprent and by Tiner (see Sprent, 1954) indicates that ascarids of carnivores behave differently (see p. 448). Beaver et al. (1952) have provided evidence that when eggs of *Toxocara canis* of dogs are swallowed by children the larvae may roam around in the liver and probably other viscera, a condition which they refer to as

visceral larva migrans; the symptoms are eosinophilia, fever, cough, and some liver enlargement. If the larvae should invade the brain they might cause very serious effects as some ascarids do in mice (p. 448), and filariae in sheep and other animals (p. 482).

After reaching the human intestine young *Ascaris lumbricoides*, 2 to 3 mm. long, grow to maturity in 2 to 2½ months. The length of life in the host is short and averages only 9 months to a year.

Epidemiology. Since a combination of heat and dryness is injurious to them, *Ascaris* eggs in feces passed on sandy soil exposed to the sun in a hot climate die before the embryos can develop. *Ascaris* thrives best where there is abundant moisture and shade and where the soil is clayish rather than sandy, since in sandy soil the sorting action of rain drops concentrates the eggs on the surface, where they are exposed to sun and desiccation (Beaver, 1952).

Infection ordinarily results from swallowing embryonated eggs, which are more frequently conveyed to the mouth by fingers than by other methods. In some places in India heavy infection is directly correlated with polluted water supplies. Brown in 1927 observed that in Panama the infection is distinctly of household nature and is derived from contamination of hands and food by eggs developing in the soil on the floors and dooryards of huts polluted by young children. In Egyptian villages the mud floors of the houses are heavily seeded with *Ascaris* eggs, and, since the Egyptian fellaheen sit, lie, eat, and play on the floor, opportunities for infection are numerous. Raw leafy vegetables, contrary to popular belief, are relatively unimportant vectors of the eggs, even in China where night soil is used for fertilizer. Considerable *Ascaris* infection may occur in the riffraff living in crowded quarters on the edges of southern cities, when there are dense shade, abundant rain, and children who are careless in their defecation habits. The playing of children on polluted ground near their homes, tracking of pollution into the houses, and eating with dirty hands are the most important factors in the epidemiology.

In the United States *Ascaris* infection is largely limited to the mountainous areas of the southeastern states and to southern Louisiana, and is concentrated in young children. Here shelter in the immediate vicinity of the dooryards leads to close-in pollution, and the clay soil is protective for the eggs.

Pathology. In heavy experimental infections the migration of the larvae through the lungs causes hemorrhages and sets up a severe pneumonia which may be fatal. The invasion may be accompanied by a fever, a temporary anemia, leucocytosis, and eosinophilia. Pigs frequently show lung symptoms known as "thumps," and similar condi-

tions have been observed in human beings preceding an *Ascaris* infection; ordinarily in nature, however, not enough eggs are ingested at a time to cause serious pneumonia.

After reaching maturity in the intestine, *Ascaris* may or may not disturb the peace of the host, but vague abdominal discomfort and acute colic pains are frequently felt, sometimes with vomiting, diarrhea, and mild elevations of temperature. Light infections may be entirely unsuspected until the eggs are found in the feces. On the other hand, the parasite is not always so docile. In heavy infections, especially if made uncomfortable by some food or drug taken by the host, the worms are likely to tangle themselves in masses and completely block the intestine. One thousand to five thousand worms have been recorded in some cases, but even less than a hundred worms may cause a blockage that is fatal if not surgically removed. A number of cases of death after carbon tetrachloride treatment for hookworm are known, due to obstruction of the intestine by squirming masses of irritated *Ascaris*.

Sometimes irritation of the mucous membranes may cause dangerous spasmodic contractions or permanent nervous constrictions of the intestine. The worms sometimes cause appendicitis by blocking the appendix. Toxic products may cause effects resembling anaphylactic shock and such nervous symptoms as convulsions, delirium, general nervousness, and coma. Sang in 1938 demonstrated a substance excreted by *Ascaris* which combines with trypsin, and he believes that when numerous *Ascaris* are present, enough destruction of trypsin may occur to interfere with digestion of proteins and account for the loss of condition and stunting of growth often seen in infected animals. Japanese workers found that *Ascaris*-infected school children were shorter than uninfected ones and had less memory and thinking capacity. Simonin in 1922 collected clinical evidence of serious effects on glands of internal secretion.

The list of dangerous complications of *Ascaris* infection is greatly enlarged by the fact that the worms have a "wanderlust" and tend to explore ducts and cavities. They frequently invade bile or pancreatic ducts and may enter the gall bladder or even go on into the liver; when children too young to have gallstones have symptoms of disease of the biliary tract, a misplaced *Ascaris* may well be suspected. Occasionally an *Ascaris* creeps forward through the stomach and is vomited or emerges through the nose of a horrified patient; it may even enter the trachea and cause suffocation. *Ascaris* sometimes passes through the intestinal wall and causes fatal peritonitis or may even come through the umbilicus or groin, or the worms may make their way into the

pleural cavity, urinogenital organs, etc. It is evident, therefore, that these worms, so far from being the "guardian angels" of children, as they were once considered, are more like bulls in a china shop.

Treatment and Prevention. *Ascaris*, as long as it stays in the intestine, is fairly easily expelled by some anthelmintics, but some, e.g., tetrachlorethylene, merely irritate the worms and cause intestinal blockage. Therefore, when different treatments for *Ascaris* and some other worm infection are indicated, the *Ascaris* treatment should usually be given first. Brown in 1946, however, found no irritating action from gentian violet.

Oil of chenopodium and Santonin are efficient drugs for ascariasis, but both are very toxic. However, a mixture of oil of chenopodium and tetrachlorethylene, as pointed out on p. 425, is usually successful. Hexylresorcinol crystals in gelatin capsules (crystoids), with fasting for 12 hours before treatment and for 4 hours afterwards, followed by sodium sulfate to expel the dead worms, is one of the most effective treatments. At a dose rate of 1 gram for adults and 0.5 gram for children, it eliminates a high percentage of the worms, and makes a clean sweep in 40 to 80 per cent of cases. Some workers recommend larger doses of 2 to 2.5 grams. Hetrazan (see p. 472), administered in a syrup, is also highly effective and non-toxic, and is particularly useful for babies and young children who cannot, or will not, swallow capsules. Hoekenga in Honduras reported 80 per cent cures with a similar dosage. Loughlin et al. (1951) recommended a single daily dose of 13 mg. per kg. for 4 days, administered in syrup. Extension of treatment to 5 or 6 days might increase the therapeutic efficacy without toxic effects.

In 1954 several workers reported a high degree of success in the treatment of *Ascaris* infections with piperazine hydrate or citrate given in a syrup, with no undesirable side reactions. On the basis of early results, 70 mg. or less per pound per day in divided doses, for 5 days, with a maximum daily dosage of 3 grams, is highly efficient.

In endemic localities treatment without sanitary improvement does little good, for a treated population usually gets back to the pretreatment level of infection within a year. On the other hand, when reinfection is stopped the worms are lost in about 9 to 12 months even without treatment. Prevention must depend mainly upon doing away with soil pollution near homes, even by very young children, and teaching children early in life to wash their hands before eating. The installation of privies is not always as successful as anticipated, because of only partial use of them. Careful washing of vegetables grown in polluted or night-soil-treated ground is desirable, for, although not

as important as soil-to-mouth infection by children's dirty hands, such vegetables may cause infection in more fastidious adults.

Other Ascaridoidea

Ascaris lumbricoides var. *suum* is a very common parasite of pigs; about 75 per cent of pigs in the United States and Canada harbor it before they are 6 months old. The principal effect is stunting of growth. Spindler found that pigs infected with 20 or more worms at 8 weeks of age failed in gain of weight, in proportion to the number of worms. One pig with 109 worms gained no weight at all, while

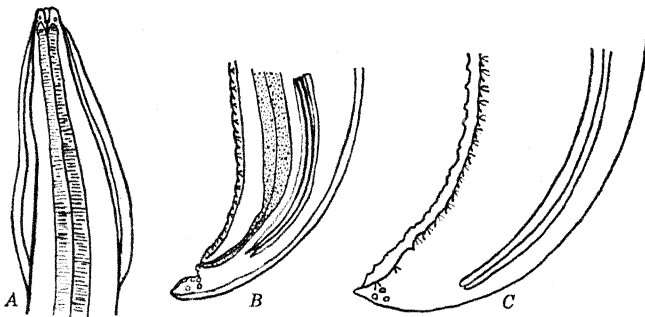


FIG. 134. A, head of *Toxocara canis*; B, tail of male of same; C, tail of male of *Toxascaris leonina*. (After Yorke and Mapleston, *Nematode Parasites of Vertebrates*, 1926.)

uninfected pigs gained an average of 100 lb. Loss results also from condemnation of carcasses for jaundice owing to blockage of bile ducts. Sodium fluoride is highly efficient for removal of *Ascaris* and stomach-worms of pigs (see p. 486) when 1 per cent is added to 1 lb. of dry ground feed for one day for a 25-lb. pig; for heavier animals additional medicated feed up to a total of 4 lb. may be given at 12- to 24-hour intervals.

Other ascarids found in domestic animals are *Parascaris equorum* (= *megalcephala*) in horses, and *Neoascaris vitulorum* in calves. Sodium fluoride at 2.5 grams per 100 lb. is effective against ascarids in horses, but may have toxic effects. Dogs and cats harbor smaller ascarids, 3 to 5 in. long, belonging to the genera *Toxocara* and *Toxascaris*. They have cervical alae which give the anterior end an arrow-head shape (Fig. 134A). *Toxocara* males have a finger-like process at the end of the tail (Fig. 134B), lacking in *Toxascaris* (Fig. 134C), and *Toxocara* eggs are delicately pitted whereas those of *Toxascaris* are smooth. Piperazine hydrate (100 mg./kg. daily for 10 days) eliminates these worms.

Toxocara apparently depends largely on prenatal infection as a means of spreading. Eggs swallowed by mother dogs migrate to the fetuses and establish themselves in their intestines; they may become encapsulated in the mother's tissues, but immunity prevents them from developing in the parental intestine. When fed to mice the larvae become encapsulated in the body tissues, and in man they cause visceral larva migrans (Beaver et al., 1952). *Toxascaris* larvae differ in migrating only into the intestinal wall of normal hosts, and in mice are encapsulated mainly in the intestinal walls. *Ascaris columnaris* of raccoons and skunks probably uses rodents as true intermediate hosts; the larvae become encapsulated in the viscera and frequently enter the brain, where even one larva may be fatal. Tiner (1953) believes brain damage may render intermediate hosts easier prey for the final hosts, and thus be of value to the parasites.

An ascarid rarely found in man is *Lagochilascaris minor*, normally found in the cloudy leopard. In several cases in Trinidad and Guiana sexually mature specimens have been found in subcutaneous or tonsillar abscesses about the head. The adults are about the size of hookworms and are identifiable by their lips and a keel-like expansion of the cuticle extending the whole length on each side.

Poultry are subject to two common types of ascarids, *Ascaridia galli* in the small intestine, and species of *Heterakis* or cecal worms in the ceca. The former, a worm about 2 to 4 in. long with a muscular preanal sucker on the male, causes retarded growth and droopiness in heavy infections in young chickens. Older birds develop a marked age immunity due to an increase in number of mucin-producing goblet cells (see p. 21). Phenyl mercuric compounds (50 mg.) plus 0.5 gram phenothiazine removes most of these worms. *Heterakis gallinarum* (= *gallinae*) is 7 to 15 mm. long with a chitin-rimmed preanal sucker and conspicuous caudal alae in the males. It seems to be harmless, even when the ends of the ceca contain swarming masses of them, except for its role as a carrier of the protozoan, *Histomonas meleagridis*, that causes "blackhead" in turkeys (see p. 127). Chickens become infected with ascarids by swallowing embryonated eggs; there is no migration through the body, but *Ascaridia* temporarily bury themselves in the intestinal wall.

Ascarids in fish-eating mammals, birds, and fish have more complicated life cycles involving first and second intermediate hosts, which are aquatic invertebrates and small aquatic vertebrates, respectively.

ASCARIDATA. II. OXYUROIDEA

As already noted, the Oxyuroidea are almost exclusively parasites of the cecum or colon of their hosts, not only of vertebrates but also of

insects. Only a single oxyurid, *Enterobius vermicularis*, occurs commonly in man.

Enterobius vermicularis

Most members of the Caucasian race, even in highly sanitized countries, fail to get through life without affording food and shelter for oxyuris, also popularly called the pinworm, seatworm or threadworm (*Enterobius vermicularis*). It is found all over the world but unlike most helminthic infections is relatively rare in the tropics. Its

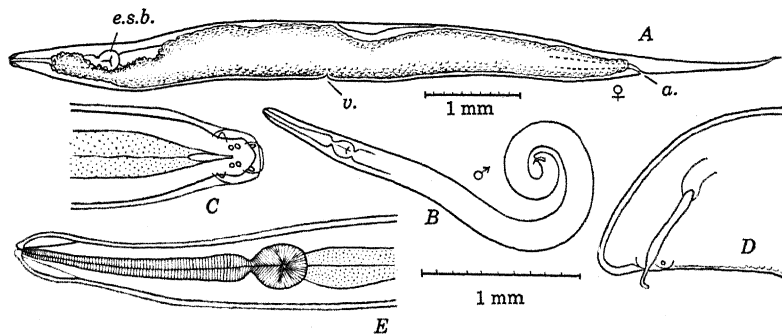


FIG. 135. *Enterobius vermicularis*. A, adult gravid ♀ (a., anus; e.s.b., esophageal bulb; v., vulva). B, adult ♂; C, posterior end of ♂, ventral view; D, same, much enlarged showing form of single spicule; E, anterior end. (C and E after Yorke and Mapleston, *Nematode Parasites of Vertebrates*, 1926.)

great stronghold is in Europe and North America, but according to Neghme 60 per cent of schoolboys in Chile are infected. As Stoll (1947) remarked, there seem to be factors in our modern way of living which are very favorable for the spread of *Enterobius* in high as well as low social levels. Sample surveys of white children in cities in the United States and Canada give incidences of 30 to 60 per cent. Colored races are far less susceptible. In Negro children in Washington, D. C., the incidence is 16 per cent as compared with 40 per cent in Whites, and in Honolulu 40 per cent in Caucasians and 21 per cent in Orientals. *Enterobius vermicularis* is strictly a human parasite, although closely related species occur in apes and monkeys.

Morphology. The adult worms (Fig. 135) live in the cecum, appendix, and neighboring parts of the intestine, from which the gravid females migrate to the rectum. These are little white worms, often seen wriggling actively in stools passed after a purge or enema. Through the semitransparent cuticle can be seen the esophagus with a bulb at its posterior end, and the uteri and coiled ovaries. The head has three small lips and is set off by lateral expansions of the cuticle. The

females, 8 to 13 mm. long, taper at both ends, but the tail is drawn out into a long, fine point. The minute males, only 2 to 5 mm. long, are less numerous than the females and are seldom noticed. The tail is curled and has a small bursa-like expansion; there is only one spicule (Fig. 135).

Life Cycle. As the uteri of the females fill with eggs, the worms migrate down to the anus; according to MacArthur (1930), they may make regular nightly trips, deposit eggs in the perianal region, and retreat into the rectum, but many worms creep out of the anus, and others are passed in the feces. Their movements cause intense itching. Contact with air stimulates the worms to deposit eggs, and a trail of these is left behind as the worms crawl. Eggs are seldom found in the feces before the worms have disintegrated but can be obtained from scrapings from about the anus or lower part of the rectum. The worms eventually dry and explode, liberating all the remaining eggs in showers. The eggs when first laid contain partially developed embryos in the "tadpole" stage, but they develop to the infective stage in as little as 6 hours. The eggs (Fig. 57Z) are clear and unstained, measuring about 55 by 30 μ , and are flattened on one side. Reardon estimated the average number of eggs in a female oxyuris to be about 11,000. After being swallowed, the larvae hatch and temporarily burrow into the mucous membranes in the region of the cecum before growing to maturity in the lumen.

Mode of Infection and Epidemiology. The eggs regain access to the same or another person in various ways, but are probably most often air-borne or conveyed by the hands. The itching caused by the emigration of the worms from the anus results in scratching, and the eggs lodged under the fingernails may eventually reach the mouth in children or others who are careless in their habits. The eggs are easily liberated into the air when sheets, clothing, etc., contaminated with them are shaken or rubbed, and may be inhaled or may settle as dust which may be inhaled later.

The extent to which the eggs become scattered in infected households is almost incredible. Not only are they present on the hands, clothing, bed linen, towels, washcloths, and soap, but also on floor, upholstery, and furniture, often in every room of houses occupied by heavily infected children. Schüffner (1944) found that the smaller the enclosed space the greater the number of eggs; in 1 square foot in a large dining hall he found 119 eggs, in a smaller classroom 305, in a toilet 5000. He pointed out that half the life of an infected child is spent in a still smaller enclosed space—between bed sheets, where the eggs are disseminated by movements of the sleeper. He believes, however, that

very heavy infections result only from transfer of eggs by fingers after scratching. Schüffner believes that chronic adult infections may be due to "retrofection," i.e., re-entrance of larvae that sometimes hatch from eggs on the perianal skin.

Cram has called attention to the familial nature of pinworm infections, and numerous observations point to its ready spread in schools and institutions. The eggs survive longest (2 to 6 days) under cool humid conditions, but their life span in dry air above 25°C. is greatly shortened, few surviving as long as 12 hours. In dry air at 36 to 37°C. less than 10 per cent survive for 3 hours and none for 16 hours. Since the worms have a life span of only 37 to 53 days, the infection would die out in this period if reinfection could be stopped; the periodic appearance of increased numbers of worms often observed at 4- or 5-week intervals is due to the maturation of new generations of worms from reinfections.

Diagnosis. No dependence can be placed upon examinations of the feces for the eggs of oxyuris. Direct fecal smears show less than 1 per cent of the actual infections, and flotation methods less than 25 per cent; even heavy infections often fail to be detected.

Far better results are obtained by scraping the perianal region. Of the several devices proposed for this, Beaver (1949) found the widely used Scotch tape method the easiest and also most efficient. A piece of Scotch tape is held by thumb and forefinger over the end of a tongue depressor, sticky side out, applied to the right and left perianal folds, and then flattened on a slide for examination. The NIH swab and wet pestle methods pick up fewer eggs and are less "foolproof." The success of these methods is affected by bathing, personal cleanliness, and irregular periodicity in the migration of the worms, so the number of eggs found has no relation to the size of the infection and one negative examination cannot be considered conclusive.

Pathology. The itching caused by migration of the worms in the anal region and by allergic irritation of the skin may be intense, causing loss of sleep, restlessness, nervousness, and even sexual disorders. In girls the worms may cause vaginitis by entering the vulva, and they may even wander into the Fallopian tubes or to the peritoneal cavity, where they become encysted.

Immature burrowing worms may cause inflammation in the cecal region, with some abdominal pain and digestive disturbances. Since the males and young females are often found in removed appendices they are often accused of causing appendicitis, but there is very little to support this view, since they are about equally common in healthy and inflamed appendices.

Treatment and Prevention. Treatment is difficult because of the situation of the worms in the cecal region far from either mouth or anus, and because if all the worms are not expelled the infection may soon build up again; this frequently happens anyway unless all the members of the family are treated.

Many of the nematode group of anthelmintics, especially tetrachlor-ethylene and hexylresorcinol, remove some of the worms. Until recently the most widely used drug has been enteric-coated capsules of gentian violet in repeated small doses of $\frac{1}{2}$ to 1 grain 3 times a day with meals or an hour before meals for 8 days or for a number of consecutive days with rest periods in between. Small $\frac{3}{20}$ - or $\frac{1}{5}$ -grain tablets are available for infants. No serious reactions develop, although some patients may lose appetite or have cramps or nausea at some time during treatment. Recently, however, two other drugs, piperazine hydrate and Terramycin, have proved at least equally as effective. Recommended dosages of Terramycin are 1 to 2 grams per day according to age, divided into 4 doses per day, for 5 to 7 days, or this dose for 2 days followed by smaller maintenance doses for 14 days. Piperazine hydrate in flavored syrup at the rate of 50 to 75 mg. per kg. per day is as effective as either gentian violet or Terramycin, without the undesirable nausea and staining of the former, or the potential harmfulness and high cost of the latter (see White and Standen, 1953). It may well become the standard treatment for pinworms. Other recent suggestions, not yet fully established, are a carbinol base of gentian violet, Lindane, Egressin, and Diphenan. The last two are derivatives of carbanilic acid. Jung and Beaver (1953) and others have got poor results with these. Another effective anthelmintic is Phenothiazine in daily divided doses totaling 0.5 to 1 gram daily for 6 to 10 days, but this sometimes causes a severe or even fatal anemia in children which develops after treatment is completed, and is therefore too dangerous for routine use.

If reinfection could be stopped the infection would disappear without treatment in a few weeks, but, even with the most meticulous care in cleanliness, complete prevention of reinfection without treatment usually fails. It requires closed pajamas of non-porous material, daily changing and sterilization of bedclothes, towels, and underwear, use of anal bandages, and disinfecting ointments, frequent washing of hands, close-clipped fingernails, a dustless house, and unrelaxing parental vigilance. Treatment is easier! Schüffner (1944) believes that 100 per cent of the children in Holland are infected in spite of the proverbial Dutch cleanliness. He thinks that efforts to eliminate the infection completely may lead to a "pinworm neurosis" that is worse than a mild pinworm infection.

In light infections a small enema of 1 or 2 ounces of water and removal of worms from the anal folds will relieve symptoms; and wearing closed bathing trunks, which will prevent picking up eggs by scratching although it will not entirely eliminate dust infection, will convert an active into a latent case. Light dust-borne infections can be minimized by using anal ointments at night and washing immediately after rising in the morning. Such methods to control rather than to completely eliminate infections in children are, in the writer's opinion, preferable to the trouble and unpleasantness of attempted treatments, until easier and more effective treatments are developed.

OTHER OXYUROIDEA

The only domestic animal that suffers from oxyuris infection is the horse, which harbors *Oxyuris equi*. Rodents harbor numerous species, and one of these, *Syphacia obvelata* of mice and rats, was found once in a child in the Philippines. Common oxyurids for class study can nearly always be found in large cockroaches.

RHABDITATA

The suborder Rhabditata is of particular interest from an evolutionary standpoint since it contains nematodes showing every imaginable gradation from free-living, saprophagous forms to strict parasites. It presents a sort of pageant of parasites in the making. The genus *Rhabditis* alone contains many species which appear to be experimenting with parasitism. Some species have been found breeding in the feces-soiled hair of the perianal region of dogs; the larvae of the common soil nematode, *R. strongyloides*, have been found repeatedly in itching pustules in the skin of dogs and other animals after lying on soiled straw bedding. Members of a related genus, *Longibucca*, have been found breeding in the stomach and intestine of snakes and bats. Another member of the same family, *Diploscapter coronata* (see p. 458), is an opportunist which is capable of establishing itself in the human stomach or female urinogenital system when abnormal conditions make these environments favorable.

Members of the families Strongyloididae and Rhabdiasidae have bridged the gap between free-living and parasitic existence by a method peculiar to themselves—a true alternation of generations. There is a free-living generation consisting of males and females which are hardly distinguishable from *Rhabditis*, and a parasitic generation of parthenogenetic females which have a markedly different appearance. The eggs produced by one generation give rise to worms of the alternate generation. This routine is, however, short-circuited by many of the individual worms by omission of the free-living bisexual generation entirely,

in spite of the fact that this is unquestionably the ancestral type. By this process we arrive at a form which is as truly parasitic as a hookworm.

The Strongyloididae pass the parasitic phase of their lives in the intestine of mammals, while the Rhabdiasidae pass theirs in the lungs of amphibians and reptiles. *Strongyloides stercoralis* is the only common and important human parasite in the Rhabditata, but *Rhabditis* (see p. 459) is frequently found in human stools, to the confusion of technicians examining them.

Strongyloides stercoralis

General Account. This, the smallest nematode parasitic in the human body except the male *Trichinella*, is a very common human parasite in moist tropical or subtropical climates, having much the same distribution as hookworms. Faust found it in 20 per cent of hospital and village populations in Panama and in 4 per cent of cases examined in New Orleans hospitals and clinics. It is a common parasite in soldiers returning from the South Pacific. Statistics based on ordinary stool examinations do not give a correct idea of the prevalence of this parasite.

The parasitic females of *Strongyloides* are parthenogenetic. Kreis (1932) and Faust (1933) found a few male worms of the free-living type in the lungs of dogs, which were undoubtedly precociously developed free-living males. There is one species of Strongyloididae, *Paraststrongyloides winchesi*, which is bisexual in the parasitic generation, but the males are filariform like the females.

The parasitic females (Fig. 136, 1) are extremely slender worms 2 to 2.5 mm. long by only 40 to 50 μ in diameter, with a bulbless esophagus about one-fourth the length of the body. The uteri diverge from the vulva in the posterior third of the body; each contains a few developing eggs in single file.

Life Cycle. (Fig. 136). The adult females burrow in the mucous membranes of the intestine anywhere from just behind the stomach to the rectum, although the upper part of the small intestine is their favorite spot. A few mature even in the bronchial tubes. The eggs, measuring about 50 by 32 μ , are deposited in the mucous membranes where they undergo development and hatch, the larvae then making their way into the lumen of the intestine, to be voided with the feces. The egg output per worm is relatively small, not more than 50 per day.

The passed larvae are rhabditiform (see p. 414) and have usually grown to a length of 300 to 800 μ . They resemble hookworm larvae but can be distinguished by the very short mouth cavity (Fig. 125, 9).

The course of development of these larvae may follow either one of two lines: (1) direct or "homogonic," or (2) indirect or "heterogonic." In the *indirect course* of development the rhabditiform larvae develop, in 36 hours or more and after four molts, into free-living males and

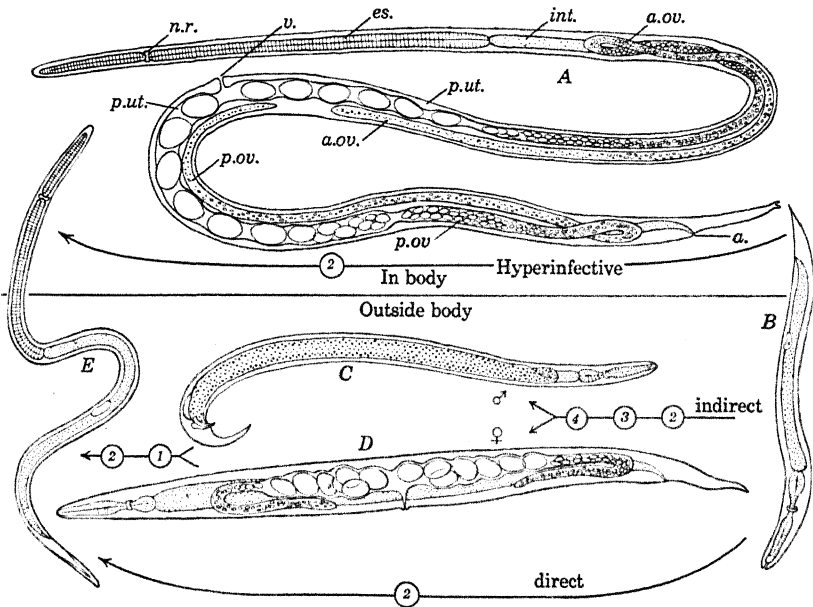


FIG. 136. *Strongyloides stercoralis*, life cycle. Direct (bottom arrow); indirect (middle arrows); hyperinfective (upper arrow). Circles enclosing numbers represent rhabditiform larval stages from 1 to 4 not drawn on diagram, and similar in appearance to B. Thus the direct cycle includes first and second rhabditiform and filariform larval stages outside body; indirect cycle includes four rhabditiform larval stages before becoming adult ♂ and ♀, then two rhabditiform stages (offspring of these) and one filariform stage before re-entering the body; hyperinfective cycle includes two rhabditiform larval stages and a filariform larval stage, all inside the body. Abbreviations: a., anus; a.ov., anterior ovary; es., esophagus; int., intestine; n.r., nerve ring; p.ov., posterior ovary; p.ut., posterior uterus; v., vulva. (Adapted from various authors.)

females (Fig. 136, 2) which closely resemble soil nematodes of the genus *Rhabditis*; they are about 1 mm. in length and 40 to 60 μ broad. These adults produce eggs which hatch into rhabditiform larvae very similar to the offspring of the parasitic females, which then ordinarily transform after two molts into slender filariform larvae characterized by a very long, slender esophagus and a long tail notched at the tip (Fig. 136E). The small, oval genital primordium is midway between the end of the esophagus and the anus. These larvae, 600 to 700 μ long, remain, like infective hookworm larvae, ensheathed by the molted

cuticles of the rhabditiform larvae, and are now in the infective stage. They may appear in less than 48 hours, and they become numerous in 5 or 6 days. They infect by penetrating the skin or mucous membranes as do hookworm larvae. Occasionally, according to Beach (1936), more than one free-living generation may develop.

In the *direct* course of development the rhabditiform larvae produced by the parasitic females, usually after a brief period of feeding and growth, metamorphose directly into infective filariform larvae at the second molt. These penetrate the skin as do those produced indirectly.

A third possible course of development, called the *hyperinfective* method, occurs in exceptional cases when the larvae of the parasitic females rapidly undergo two molts inside the intestine without feeding or growing, transforming into filariform larvae which then burrow through the mucous membranes or perianal skin, causing reinfection without any outside existence (see Faust and de Groat, 1940).

The larvae of *Strongyloides* are easily destroyed by cold, desiccation, or direct sunlight, and are rather short-lived even under the most favorable conditions. This probably accounts for the infrequency of *Strongyloides* infections outside warm moist climates.

After penetration some larvae remain in the skin for a long time, but they appear in the lungs from the third day onward. The larvae undergo development to adolescence in the lungs, and then migrate to the alimentary canal via the trachea and throat, although a few mature and reproduce in the lungs and bronchioles. Larvae begin to appear in the feces about 17 days or more after infection in man, but in dogs the prepatent period is only 12 days and in rats 6 days. The numbers rise rapidly but decrease again after some months, when immunity begins to develop.

Biology of Direct and Indirect Development. The apparently willy-nilly appearance of the direct and indirect modes of development of *Strongyloides* has been very puzzling. Attempts have been made to explain it on the basis of environmental effects inside and outside the host, age of worms, fertilization by supposed parasitic males, and biologically different strains. Graham (1936-1939) started two pure lines of *S. ratti* in rats from original single-larva infections of the homogonic and heterogonic types, respectively, and found marked inherent differences between them. In each line over 85 per cent of the total progeny were of its own type, with an extreme difference in the number of free-living males produced. Meanwhile Beach (1935, 1936) showed conclusively that the course of development can be influenced by nutritional conditions; as these become less favorable more and more of the

rhabditiform larvae undergo direct transformation into filariform larvae instead of becoming males and females. The conclusion seems warranted, therefore, that the course of development is dependent upon nutrition or other environmental influences and not on genetic constitution, but that there are genetic differences in the extent to which different strains are influenced toward homogeneity by given degrees of unfavorableness in the environment.

Diagnosis. The infection is diagnosed by the finding and identification of the larvae in the stools; they can be found in simple fecal smears and can be floated satisfactorily in zinc sulfate solution (see p. 256), but they shrink badly in saturated sodium chloride. If scanty they can be found readily by culturing the stool mixed with an equal part of charcoal or sterilized earth. The rhabditiform larvae, as already noted, can be distinguished from those of hookworms by the very short mouth cavity, but are difficult to distinguish from coprophagic *Rhabditis* larvae in stale or contaminated stools unless cultured for 2 to 5 days, and the filariform larvae found by extraction into warm water. Embryonated eggs are occasionally found in cases of severe diarrhea. In examining stale stools there may be confusion with hookworm infections, but an excess of larvae over eggs in uncultured stools is indicative of *Strongyloides*. The eggs, if present, are decidedly smaller and always embryonated.

Pathology. Skin penetration by the larvae often causes redness and intense itching, with lesions resembling ground itch. Invasion of the lungs sometimes causes acute inflammation. The adults burrowing in the intestinal mucosa cause a catarrhal inflammation with so much erosion in severe cases as to give the appearance of raw beefsteak. In very light infections there may be no demonstrable symptoms; in moderate and chronic cases there are usually intermittent diarrhea and epigastric pain; in severe cases there may be uncontrollable diarrhea with blood and undigested food in the liquid stools. The loss of food and continued drain of liquids cause severe emaciation. In the tropics there is often evidence of allergic effects as well. de Langen described cases in Java with high eosinophilia, leucocytosis, anemia, slight fever, edema, and bronchial pneumonia in addition to the intestinal symptoms, and Faust called attention to the frequency of nervous symptoms in chronic infections. These are probably due to toxic allergic effects of disintegration of numerous larvae invading the bodies of people who have been repeatedly exposed.

Treatment and Prevention. Gentian violet is moderately effective for *Strongyloides* infections. It stains the intestinal mucosa and kills some, but usually not all, of the adult worms buried in it. The

standard treatment for adults is two $\frac{1}{2}$ -grain enteric-coated tablets (to open in $1\frac{1}{2}$ hr.) with meals three times a day for 16 days; for children the dosage is 9 mg. per day per year of age. The difficulty is to get the tablets to open where needed in the duodenum but not in the stomach. Administration of 25 cc. of a 1 per cent aqueous solution of gentian violet by duodenal tube may be effective in refractory cases, or even 25 cc. of a 0.5 per cent solution intravenously. Hexylresorcinol is very toxic to *Strongyloides* in vitro but may not be effective in vivo. Hetrazan by stomach tube was reported to have given favorable results.

Control is much the same as in hookworm infections, except that the delicacy of the *Strongyloides* larvae should make it easier.

***Strongyloides* in Animals.** *Strongyloides stercoralis* is infective for dogs and cats as well as man but usually dies out in a number of weeks. In India, however, the writer found a high percentage of cats naturally infected with a *Strongyloides* which was very similar to, if not identical with, the human species. Other species occur in monkeys, sheep, rodents, pigs, and other animals. One human infection with *S. fülleborni* of monkeys has been reported. Most of the species in herbivorous animals differ from those in man and carnivores in that the eggs usually do not hatch until after they have left the body of the host.

Diploscapter coronata

Some nematodes found in the aspirated stomach contents of nine patients who were suffering from complete or almost complete lack of hydrochloric acid were examined by the writer (1938) and found to be *Diploscapter coronata* (Fig. 137). This nematode was previously

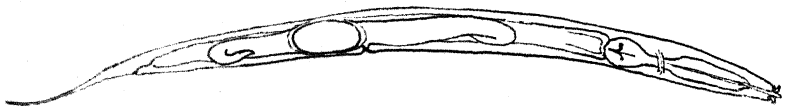


FIG. 137. *Diploscapter coronata*, adult female from human stomach. (After Chandler, *Parasitology*, 1938.)

known only as an inhabitant of soil or sewage beds; a related species is parasitic on living roots of plants. The worms from the stomach were abundant in some cases and scanty in others; they were in all stages of development, but no males were found. This corresponds with most previous observations on this worm; apparently, like *Strongyloides* and some species of *Rhabditis*, it can get along very well without the presence of the male sex. Adult females are about $420\ \mu$ long.

All the cases were discovered in a Houston clinic, and similar cases

are reported as having been seen frequently before, but incorrectly diagnosed as *Strongyloides*. In one case a re-examination 4 days later showed the worms still present, so they were undoubtedly established in the stomach. Oddly enough, only a single prior case of similar nature has been recorded in the literature. The same worm has, however, been found in the urine of women, once in Japan and three times in Israel.

Rhabditis

The genus *Rhabditis* contains numerous species of nematodes normally found in soil, organic matter, or water, and frequently in feces of man or animals. They closely resemble the free-living generation of *Strongyloides* but have no alternation of generations.

Rhabditis pellio is a species which has on a few occasions been found living in the human vagina, the larvae escaping in the urine. *R. hominis* and other species have been recorded from stools of man and animals. In most of these cases there was suspicion of their being true parasites, but the worms have not been found on re-examination, and in some cases clear evidence of contamination with soil or water was obtained. There is as yet no conclusive evidence that any of these species are more than coprophagous. Other pseudo-infections with *Rhabditis* were mentioned on p. 453. Their only importance is their possible confusion with *Strongyloides*.

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Filariae, Spiruroids, and Guinea Worm

SUBORDER SPIRURATA. I. FILARIAE (SUPERFAMILY FILARIOIDEA)

The filariae, constituting the superfamily Filarioidea of the suborder Spirurata (see p. 390) are slender thread-like worms which inhabit some part of the blood or lymphatic system, connective tissues, body cavities, eye sockets, nasal cavities, etc. They have simple mouths without lips and rarely a vestibule; the females nearly always have the vulva forward near the mouth, and the relatively small males have spirally coiled tails, with or without alae but always with papillae. Many of them—all those that concern us here except *Parafilaria* in horses—produce embryos that live in the blood or skin, whence they are sucked out by bloodsucking arthropods which serve as intermediate hosts; they gain access to a new host through the skin when these arthropods bite.

The classification into families and subfamilies is still controversial. We shall follow Wehr's (1935) arrangement, as modified by Chabaud and Choquet (1953), who divided one of the families, Dipetalonematidae, into six instead of two subfamilies. Wehr recognized four families; of these three, Stephanofilariidae, Filariidae, and Dipetalonematidae, contain parasites of medical or veterinary interest. The first contains a single genus, *Stephanofilaria*, a skin parasite of horses, cattle, etc., with a row of small spines around the mouth. The other two, Filariidae and Dipetalonematidae, are distinguished mainly by the first-stage larvae, which are usually short and stout with spiny anterior ends in the Filariidae and long and slender with no spines in the Dipetalonematidae. Except *Parafilaria* and *Setaria* in horses and cattle, all the species parasitic in man or domestic animals belong to the Dipetalonematidae, distributed in three of the six subfamilies. The Dirofilariinae, with short tail, well-developed caudal alae in the males, and esophagus externally divided into separate muscular and glandular parts, contains *Loa* and

Dirofilaria; the Dipetalonematinae, with long tail, very narrow caudal alae, if any, in the males, and no external division of the esophagus, contains *Wuchereria*, *Dipetalonema*, and *Mansonella*; and the Onchocercinae, with short tail, inconspicuous alae, and undivided esophagus, contains *Onchocerca*.

Guinea worms, *Dracunculus*, were formerly classed with filariae but are now placed in an entirely distinct suborder (see p. 490). At one time all the filariae were placed in the single genus *Filaria* and are sometimes still so referred to in medical and veterinary books.

Microfilariae. Many filarial infections are practically impossible to diagnose except by the embryos or "microfilariae," and it is therefore important to be able to distinguish these. When living they are colorless and transparent and may or may not be enclosed in "sheaths." In order to identify them it is usually necessary to stain them. The body will then be found to contain a column of nuclei, broken in definite places which serve as landmarks (Fig. 138). The principal ones are a nerve ring anteriorly, an excretory pore or "V" spot, an excretory cell somewhat farther back, a few genital cells posteriorly, and an anal pore or "tail spot." The spacing of these landmarks is fairly constant in different species. The presence or absence and arrangement of nuclei in the head and tail ends and the shape of the tail are also useful identification marks. The following table shows the outstanding characters of the microfilariae found in human blood or skin (see also Fig. 138).

Sheathed forms.

Mf. bancrofti: about 225 to 300 μ by 10 μ ; sheath stains red with dilute Giemsa stain; tail end tapers evenly; no nuclei in tail; does not stain with 1 : 1000 methylene blue when alive; lies in graceful coils when dried; nocturnal or non-periodic; in blood or urine.

Mf. loa: same size; sheath unstained in Giemsa; tail short and recurved, with nuclei to tip; stains with methylene blue when alive; lies in kinky scrawls when dried; diurnal; in blood.

Mf. malayi: about 160 to 230 μ by 5 to 6 μ ; tail sharp-pointed, with a single nucleus at its tip and another 10 μ in front of it; nocturnal.

Unsheathed forms.

Mf. perstans: about 200 μ by 4 μ ; tail ends bluntly, with nuclei to its tip; stains with methylene blue when alive; no periodicity; in blood.

Mf. streptocerca: about 215 μ by 3 μ ; tail ends in a crook and terminates bluntly with nuclei to tip; does not stain with methylene blue when alive; no periodicity; in skin.

Mf. ozzardi: about 200 μ by 5 μ ; tail sharply pointed, with no nuclei at its tip; stains with methylene blue when alive; no periodicity; in blood.

Mf. volvulus: about 300 to 350 μ by 5 to 8 μ ; tail sharply pointed, with no nuclei at its tip; no periodicity; in skin.

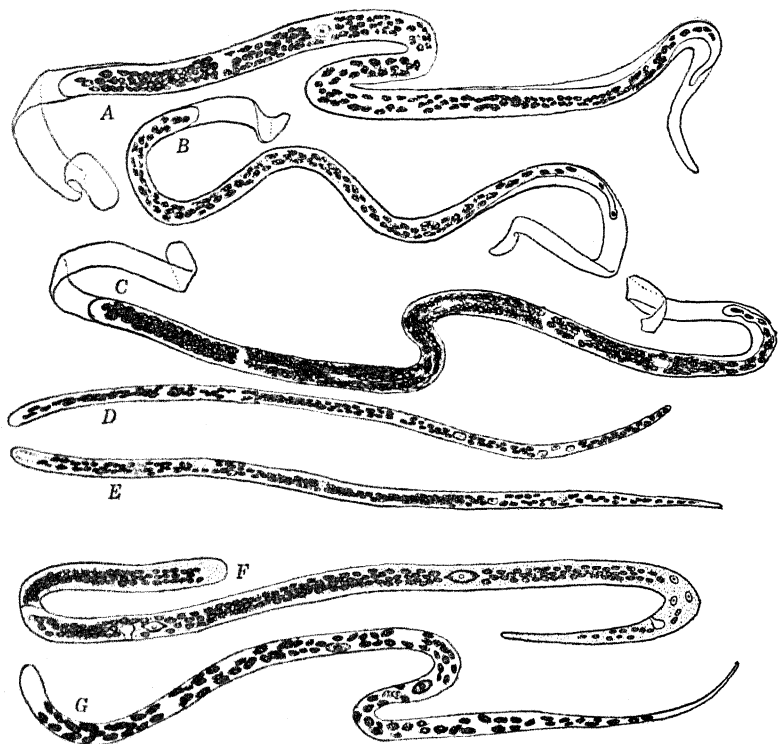


FIG. 138. Various species of microfilariae drawn to scale.

A, *Wuchereria bancrofti*; sheathed, no nuclei in tip of tail, $270 \times 8.5 \mu$.

B, *W. malayi*; sheathed, 2 nuclei in tail, $200 \times 6 \mu$.

C, *Loa loa*; sheathed, nuclei to tip of tail, $275 \times 7 \mu$.

D, *Dipetalonema perstans*; no sheath, tail blunt with nuclei to tip, 200 to 4.5μ .

E, *Mansonella ozzardi*; no sheath, pointed tail without nuclei at tip, $205 \times 5 \mu$.

F, *Onchocerca volvulus*; no sheath, no nuclei in end of tail, $320 \times 7.5 \mu$.

G, *Dirofilaria immitis*; no sheath, sharp tail without nuclei in end, $300 \times 6 \mu$.

Wuchereria (Filaria) bancrofti

Distribution. This worm is a very widespread and important human parasite in warm countries but is not evenly distributed or uniformly prevalent throughout any country. As Augustine (1945) pointed out, it occurs almost entirely in coastal areas and islands where there is a fairly long hot season with high humidity. In Africa it is found on the Mediterranean and east and west coastal areas but not in the interior of Central Africa. In Asia it is prevalent on the coasts of Arabia, India, Malaya, and north to China and the southern parts of Korea and Japan. It is prevalent in practically all the East Indian and South Pacific islands and on the coasts of Queensland.

In the Western Hemisphere, where it was almost certainly introduced by Whites or Negroes, it is prevalent throughout the West Indies and on the northern coast of South America from northern Brazil to Colombia, but it is strangely scarce or absent on the Caribbean shores of Central and North America. In the United States it was once endemic in Charleston, S. C., but failed to become established elsewhere and has apparently died out there. Throughout this area it is almost completely restricted to towns and sometimes even to parts of them, but in some places it affects 80 per cent or more of the local population.

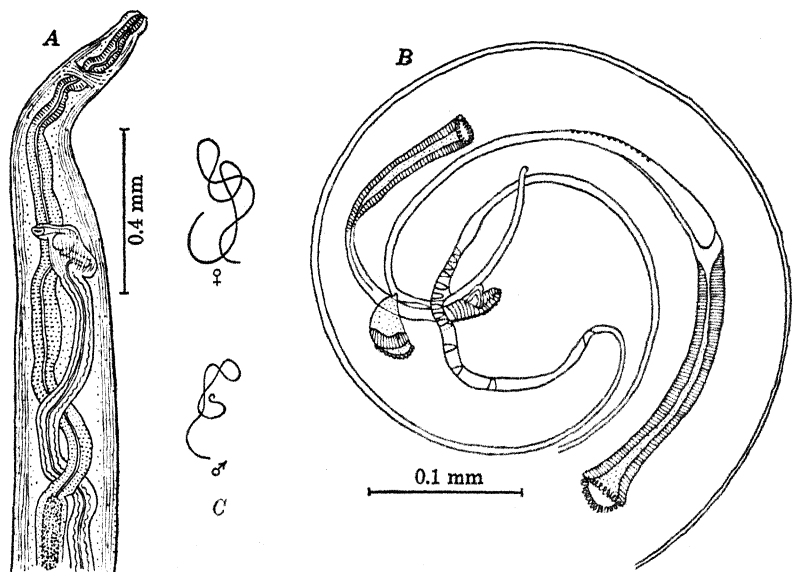


FIG. 139. *Wuchereria bancrofti*. A, anterior end of ♀; B, posterior end of ♂; C, adult ♀ and ♂, natural size. (A, after Vogel, *Arch. Schiffs- u. Trop.-Hyg.*, 32, 1928; B, after Fain, *Ann. parasitol. hum. et comp.*, 26, 1951.)

Morphology. The adult worms (Fig. 139) live in the lymph glands or ducts, often in inextricable tangles. The females are 65 to 100 mm. long and only 0.25 mm. in diameter—about the caliber of coarse sewing thread; the males are about 40 mm. long and 0.1 mm. in diameter. The body tapers to a fine head slightly swollen at the end, with a simple pore as a mouth. The esophagus is partly muscular and partly glandular, with the vulva opening a little behind its middle. The males have the tail coiled like the tendril of a vine, with numerous pairs of papillae; there is one long and one short spicule.

Life Cycle. The female worms give birth to microfilariae which are surrounded by delicate membranes or sheaths. Other characters are

listed on p. 463. These microfilariae appear in the peripheral circulation chiefly between 10 P.M. and 4 A.M., except in the non-periodic variety *pacifica* (see below).

There has been much speculation and experiment to determine the reason for this periodicity. One theory was that the larvae are concentrated in internal organs during the day, and circulate in the blood at night to keep a sort of tryst with their night-biting mosquito transmitters, chiefly *Culex fatigans* or *C. pipiens* and certain species of *Anopheles*. Another theory was that the embryos are born at a certain time each day, and are then destroyed in the host within the next 24 hours. Recently Hawking and Thurston (1951) reviewed this matter and gave convincing evidence that, at least in the case of some filarial infections in monkeys and dogs, the microfilariae are concentrated mainly in the capillaries and other blood vessels of the lungs when not present in the peripheral circulation. The stimulus which induces the microfilariae to enter the general circulation is connected with periods of activity of the host, for it is gradually reversed in people who reverse their sleeping and working hours, or go half way around the world.

Throughout the greater part of the range of *Wuchereria bancrofti* the microfilariae have nocturnal periodicity, i.e., appear in numbers in the peripheral circulation only at night, but in the Polynesian Islands (Samoa, Fiji, Tonga, and Cook Islands) there is a non-periodic variety, with different transmitters and epidemiology, and differing somewhat in its pathogenic effects. In the Philippines this form co-exists with the usual "periodic" form. Although the non-periodic form is not morphologically distinguishable except for a slightly greater length of the adults, this form may properly be recognized as a variety or subspecies *pacifica*; Manson-Bahr and Muggleton (1952) think it deserves to be considered a distinct species.

The further development of the microfilariae depends on their being sucked with blood by certain species of mosquitoes which serve as intermediate hosts (see p. 730). Unlike malaria and yellow fever, *Wuchereria bancrofti* is not limited to transmission by species of one genus or group of mosquitoes; it is transmitted by certain species of *Culex*, *Aedes*, *Anopheles*, and others. *Culex fatigans* (= *quinquefasciatus*) and in some places the closely related *C. pipiens* play a leading role as vectors of the periodic form in most parts of the world, but these are replaced by certain *Anopheles* in some places. *Aedes scutellaris* var. *polynesiensis* is the principal vector of the non-periodic type except in Fiji. *C. fatigans* is highly refractory as a transmitter of the non-periodic form. For further details on transmitters see pp. 730-731.

In order to infect mosquitoes there must be about 15 or more microfilariae per drop of blood (20 cu. mm.); a high concentration of 100 or more per drop is fatal to the mosquitoes. Sometimes the blood contains up to 600 in a drop.

Shortly after being ingested by a mosquito the embryos penetrate through the stomach wall and migrate to the breast muscles, where they lie lengthwise between the muscle fibers (Fig. 140A). Here the

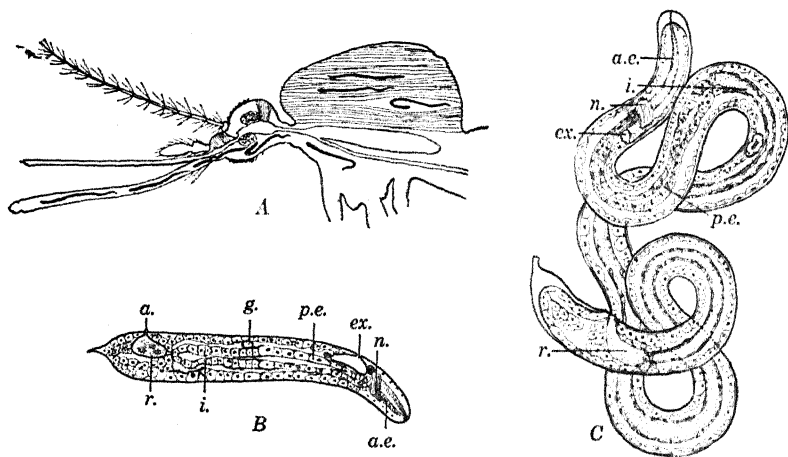


FIG. 140. *Wuchereria bancrofti*. A, mature larvae in thoracic muscles and proboscis of a mosquito (adapted from Castellani and Chalmers). B, "sausage" stage of development of larva in thoracic muscles; C, infective larva from mosquito proboscis (adapted from Looss). Abbreviations: a., anus; a.e., anterior portion of esophagus; ex., excretory pore; g., genital rudiment; i., intestine; n., nerve ring; p.e., posterior portion of esophagus; r., rectum.

body shortens to half its original length but grows several times as thick, thus changing into a sausage-shaped creature (Fig. 140B). Then the digestive tract differentiates, and the worms begin to grow in length as well as girth, eventually measuring about 1.5 to 2 mm. by 20 to 30 μ (Fig. 140C). During this time there have been two molts and the larvae have reached the infective stage. They now leave the thoracic muscles to make their way towards the head of the mosquito and down into the proboscis in the interior of the labium, although some get lost and end up in other parts of the body.

This development to the infective stage takes a minimum of 8 to 10 days but more frequently 2 weeks or more. The optimum conditions are 80°F. and 90 per cent humidity. At best only a small percentage of the microfilariae ingested develop into infective larvae.

When the mosquito bites a warm moist skin the larvae break free from the labium where the labellum is joined, creep out on the skin of the host, and penetrate through the mosquito bite or other abrasions. This happens successfully only in warm moist weather, for cold makes the larvae inert and dryness destroys them. Gradually, as the mosquitoes bite, the larvae escape from the proboscis until after about 3 weeks all are gone.

Nothing is known of the course pursued by the larvae after they enter the skin and very little as to the time required for sexual maturity to be reached. The large heart filaria of the dog, *Dirofilaria immitis*, matures 9 months after infection, and it is unlikely that the human filaria takes longer. The fact that in India children seldom show microfilariae in their blood under 5 years of age and Europeans only after many years of residence in an infected locality is due either to the scarcity of the embryos in the blood or to failure of the males and females to meet each other in the same glands or lymph ducts. Probably the adults live at least 4 or 5 years.

Pathology. Filarial symptoms are caused by the adult worms; the microfilariae usually produce no symptoms. The so-called signs and symptoms are due either to inflammatory reactions or to lymphatic obstruction.

It is very likely that the inflammatory effects are due largely to allergic reactions in sensitized tissues. They consist primarily in inflammation of lymph glands (lymphadenitis) and lymph channels (lymphangitis), particularly of the male genital organs (scrotum, spermatic cords, epididymis, and testes), and of the arms and legs. The attacks are usually recurrent, often being precipitated by exercise, and may be accompanied by chills, fever, aches, and general malaise. It is believed that the allergic irritation may be due either to fluid in which the embryos of the worms are discharged, or other metabolic products, or to proteins liberated from dead and phagocytized worms. Some workers, e.g., Grace, believe that hypersensitiveness to accompanying chronic *Streptococcus* infections is largely responsible for the symptoms. Failure of penicillin and sulfonamides to affect filarial lymphangitis is against this theory.

Obstruction of lymph channels may play a prominent part in the symptoms, especially in old infections. The dramatic end result of this is elephantiasis (Fig. 141), which, as Brown (1945) says, is popularly but mistakenly believed to be the inevitable final termination of every filarial infection. This belief caused a tremendous amount of unnecessary mental anguish and psychoneurosis during World War II among infected American troops in the South Pacific, who had visions

of themselves ending up with anything from sterility to being attached to a 200-pound scrotum or leg.

The earliest obstructive effects are varicose lymph or chyle vessels behind places where lymph glands or channels are blocked by inflammatory tissue reactions. Such varices may burst and divert large

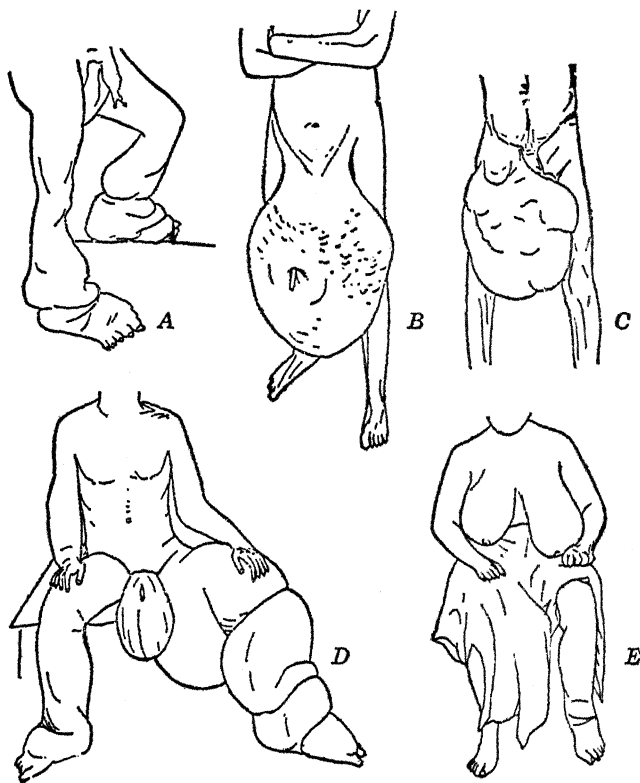


FIG. 141. Some extreme cases of elephantiasis. *A*, of legs and feet; *B*, of scrotum; *C*, varicose groin gland; *D*, scrotum and legs; *E*, of mammary glands. (*A* and *B* sketched from photographs from Castellani and Chalmers; *C*, *D*, and *E* from Manson.)

amounts of lymph or chyle into the scrotum, bladder, kidney, or peritoneum, or even into the intestine. When obstruction occurs in the smaller lymph channels in the subcutaneous system and skin, especially in scrotum, limbs, breast, or vulva, the tissues become swollen and "blubbery." Eventually fibrous tissue increases and the skin becomes dense, hard, and dry, since the sweat glands also degenerate. This process may gradually increase until true elephantiasis appears, when

certain parts of the body develop to monstrous proportions. It is a characteristic feature of obstructive forms of filariasis that microfilariae are commonly absent from the blood, either because they are dammed up in the lymph system or because the parental worms have died. There is a positive correlation between incidence of filarial disease and microfilaria rate in a community but a negative correlation between elephantiasis and blood microfilariae in an individual.

As Brown pointed out, any disease that may run its course for a period as long as 50 years is likely to vary greatly in its clinical course in different human hosts. Such factors as number of worms, speed with which they are acquired, and allergic sensitivity of the individual must be taken into account. Many cases never show any obvious symptoms. In a large group in the Virgin Islands, 20 per cent had microfilariae in the blood, yet practically all were unaware of infection. One had 23,240 microfilariae per cc. of blood yet had no signs or symptoms of filarial infection except a slight general glandular enlargement.

It has been common experience in India and other parts of the world that filarial symptoms are slow in appearing; in India, Europeans seldom show symptoms until they have resided in endemic localities for 10 to 15 years, and even native children seldom show symptoms until half grown. Sometimes, however, elephantiasis, once started, may develop rapidly. Brown saw a patient whose scrotum grew from normal size to a weight of 14 pounds in a year.

In contrast to all prior experience with filariasis, American troops exposed to the non-periodic strain in Samoa and other South Pacific islands during World War II developed filarial symptoms in as short a time as 3½ to 6 months and in an average of 9 months (Dickson, Huntington, and Eichold, 1943). This disease, called by the native name "mu-mu," was characterized by lymphangitis, enlarged glands, swelling, and redness, most frequently in the genitals or arms and less often in the legs. Headache, backache, fatigue, and nausea were common, but fever and malaise were unusual; physical and mental depression was very pronounced. Microfilariae appeared in the blood in very few cases.

It seems probable that the differences between this rapidly developing disease and the slow-developing filariasis of other parts of the world was due to intensity of infection and consequent early development of strong allergic reaction. In most places in the tropics Europeans are segregated from infected natives at night and protect themselves from mosquitoes sufficiently to escape heavy infections. In the Pacific islands, where the abundant day-biting *Aedes scutellaris polynesiensis* is the transmitter, men working or fighting in or near native

villages may get as many infective bites in a month as they would get in India in years. A very interesting and possibly significant fact is that in islands where only the nocturnal strain exists, e.g., North Guinea, few or no cases developed among white troops.

Little work has been done on immunity to filarial infections, but work by Scott and McDonald (1953) on *Litomosoides* in cotton rats indicates that as in other worm infections immunity is directed against metabolic products of the worms rather than against the body proteins (see p. 23).

Diagnosis. If microfilariae are present they can usually be demonstrated (in night blood in the nocturnal strain) by examination of a fresh drop of blood for squirming microfilariae, or of a dehemoglobinized and stained thick smear (see p. 204). A more accurate method in case the embryos are scanty is to take 1 cc. of blood in 10 cc. of 2 per cent formalin, centrifuge, and examine the sediment. For specific identification the embryos should be stained by Giemsa or Wright methods.

Since microfilariae are frequently absent, especially in elephantiasis cases, clinical signs and symptoms must be relied on to a considerable extent. Skin tests with antigen prepared from *Dirofilaria immitis* or other filariae, since there is very little specificity, are very helpful. Injection of 0.01 cc. of a 1 : 8000 dilution gives positive reactions in most cases and a minimum of false positives, though many of the positives are not clinically active cases. False positives are probably due, as Augustine and Lherisson (1946) pointed out, to sensitization of man by larvae of non-human filarial worms, to which he must often be exposed. Negative skin reactions are helpful in ruling out filarial infections, though they sometimes occur in active cases, probably due to desensitization (Huntington, 1945).

Treatment and Prevention. Filariasis apparently balked all efforts to treat it until World War II, when several American workers (Brown, 1944, and Culbertson et al., 1945, 1947), following up successful experiments on *Dirofilaria* in dogs and on *Litomosoides* in cotton rats, found that a number of antimony and arsenic compounds given over a period of 2 weeks or more greatly reduced or completely eliminated the infections. The antimony compounds (especially Neostibosan) quickly kill the microfilariae but have slower effects on the adults; the latter have their reproductive organs injured, resulting in eventual sterility as in the case of antimony-treated schistosomes, but the response in some cases is disappointing. The arsenic drugs, of which arsenamide is most promising, have a slower effect on the microfilariae, but kill or sterilize the adult worms rather quickly. Arsenamide has been found very

effective against both the periodic form of *W. bancrofti* (in Virgin Islands) and the non-periodic form (in Samoa) (Otto, Brown et al., 1952; Otto et al., 1953), but has the disadvantage of having to be given intravenously daily for 15 days. The minimum curative dose is probably 0.6 mg. per kg. daily for at least 10 to 12 days. The diarrhea and nausea which it sometimes causes can be relieved by giving ascorbic acid.

Hetrazan, a piperazine derivative given by mouth, very rapidly kills the microfilariae, and probably has a slow and gradual effect on the adult worms. The microfilariae disappear completely or nearly completely in a few hours and often fail to reappear for many months, whereupon they gradually return. In Samoa, however, Otto et al. found a number of treated cases showing few microfilariae, sometimes none, even after 2 years. Evidently in these cases the adult worms were either destroyed or sterilized. The dosage used is 3 mg. per kg. body weight daily for 7 to 14 days. The principal disadvantage is that allergic symptoms always develop as the result of the sudden destruction of the microfilariae and liberation of their proteins in a sensitized body. The symptoms vary from brief chills and fever to almost complete prostration with severe headache, muscular aches, dizziness, sweating, etc. Suramin (Bayer 205 or Antrypol) also has some effect on *Wuchereria* infections, but is too toxic for routine use.

Some workers believe that elephantiasis is brought on by dead filariae, so the wisdom of killing the adult worms by chemotherapy has been questioned; but no evidence of elephantiasis has appeared in cured patients. In some cases of elephantiasis Knott (1938) has obtained good results from pressure bandaging. In some cases surgery can be used to advantage, as Auchincloss showed in 1930. Cortisone (100 mg. daily for several weeks) is at least temporarily helpful.

Control is largely a matter of mosquito control, and this varies with the local transmitters. The predominantly urban *Culex fatigans* can be controlled by local elimination of breeding places and DDT spraying; the latter is also effective against some of the *Anopheles* transmitters. The *Aedes* of the *scutellaris* group that transmit the variety *pacifica*, on the other hand, seldom enter houses and almost never rest in them, so they cannot be controlled by DDT. Here wholesale use of Hetrazan to eliminate most of the microfilariae may be the best solution.

Wuchereria malayi

Although *Wuchereria bancrofti* was long thought to be the only filaria that was commonly responsible for lymphangitis and elephantia-

sis, it has been found that in many places this species plays a very subdued second fiddle to another species that was long known only by the embryo, *Microfilaria malayi* (see p. 463 and Fig. 138B). The adults, which resemble *W. bancrofti* closely, were first found by Rao and Maplestone (1940) in India.

W. malayi is common in many places in India and in southeastern Asia and the East Indies, sometimes along with *bancrofti*, sometimes alone; it may affect up to 50 per cent of the rural population.

The transmitting mosquitoes are mainly species of *Mansonia* (see p. 731). Since these live in swamps, with the larvae and pupae attached to the roots of water plants, the disease is strictly rural. *W. bancrofti* infections increase toward the center of towns, *malayi* infections peripherally. In India *Mansonia annulifera* is the principal vector, and so the disease can be controlled by the delightfully simple method of removing *Pistia* (water lettuce) on which this mosquito lives almost exclusively (Iyengar, 1938). In Malaya, however, the chief vector is *M. longipalpis*, which pierces the fine roots of swamp-loving trees, and so only extensive drainage is effective.

The pathogenic effects of *malayi* infection are similar in most respects to those of *bancrofti* infection, but the elephantiasis is more frequently in the legs, and the genital organs are rarely affected. In Travancore, microfilariae were occasionally found in children only 2 years old, and elephantiasis was seen in a child of 6. In military personnel repatriated from Indo-China, a condition of "tropical eosinophilia," with swelling and inflammation of lymph glands and bronchial and pneumonic symptoms, has been observed.

The African Eye Worm, *Loa loa*

This worm is a common parasite in west and central Africa. The same or a closely related species has been found a few times in monkeys. The adults live in the subcutaneous tissue of man and make excursions from place to place under the skin, causing itching and a creeping sensation; they show a special preference for creeping in and about the eyes (Fig. 142D), and are responsive to warmth. In a person sitting before a fire the worms become active and move to exposed parts; they have been observed to travel at the rate of about an inch in 2 minutes.

The adult worms resemble pieces of surgical catgut, the female varying from about 20 to 70 mm. in length, whereas the males measure about 20 to 35 mm. The general anatomy is not unlike that of *Wuchereria bancrofti*, but the cuticle is provided with numerous little dewdrop-like warts along the lateral lines (Fig. 142).

Loa loa produces sheathed embryos (see p. 463 and Fig. 138C) which make their way to the blood stream. They have a diurnal periodicity, swarming in the blood in the daytime and disappearing at night. The intermediate hosts are certain species of *Chrysops* (*C. dimidiata*, *C. silacea*, and possibly others), known as mango flies (see p. 670). The larvae develop in the fly's abdomen, sometimes by hundreds, and invade the proboscis after development to the infective stage, which takes 10 to 12 days. When the fly bites, the larvae file out of the proboscis and enter the skin through the bite.

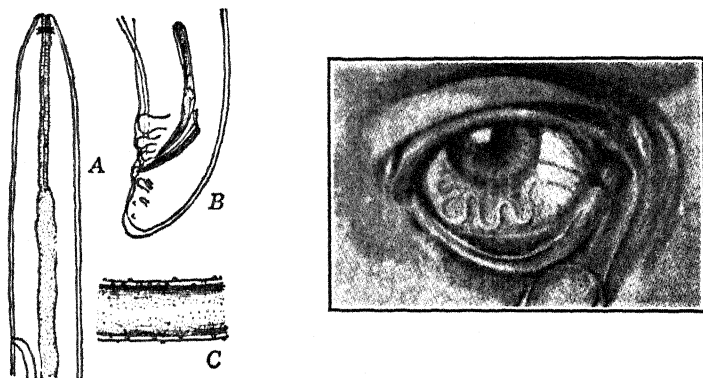


FIG. 142. *Loa loa*: A, anterior end, showing muscular and glandular parts of esophagus and position of vulva ($\times 20$); B, tail of male, showing spicules, narrow alae, and papillae ($\times 100$); C, portion of body showing dewdrop-like warts on cuticle along lateral lines; D, *Loa loa* in eye. (A, B, and C adapted from various authors; D, after Fülleborn in Kolle u. Wassermann, *Handbuch der path. Mikroorg.*, Vol. 6, 1929.)

Loa worms seem especially active in their youth, later showing a tendency to retire to deeper parts of the body. In the eye they are painful, but it is here that they can most easily be extracted. The extraction, however, has to be done expeditiously, before the disturbed worm flees to hiding places deeper in the body.

Loa infections are usually accompanied by painless though sometimes itchy edematous swellings, commonly as large as pigeon eggs, which appear suddenly, last a few days, and then disappear to reappear later somewhere else. These "Calabar swellings" are often more troublesome a few months after removal to a cold climate than they are in West Africa, so much so that they take the joy out of leave trips home for some Europeans. The swellings are undoubtedly allergic reactions to metabolic products of the worms or to proteins liberated from injured or expired worms. Chandler, Milliken, and Schuhardt

(1930) produced a large swelling by injection of a minute amount of *Dirofilaria* antigen into the skin of a patient. Kivits (1953) reported *Loa* microfilariae in the cerebrospinal fluid in four cases of fatal encephalitis. Possibly the microfilariae cause serious effects when they penetrate into the brain or spinal cord, as do *Setaria* larvae (p. 482), or perhaps they open the door for neurotropic viruses or even carry them in.

Hetrazan, even in small doses, kills the microfilariae of *Loa*, and relieves symptoms, but affects the adults slowly if at all.

***Dipetalonema* (= *Acanthocheilonema*) *perstans* and
*D. streptocerca***

The genus *Dipetalonema* (including the old genus *Acanthocheilonema*), contains many species found in monkeys and small animals. *D. perstans* (Fig. 143) is a very common parasite of man and apes in

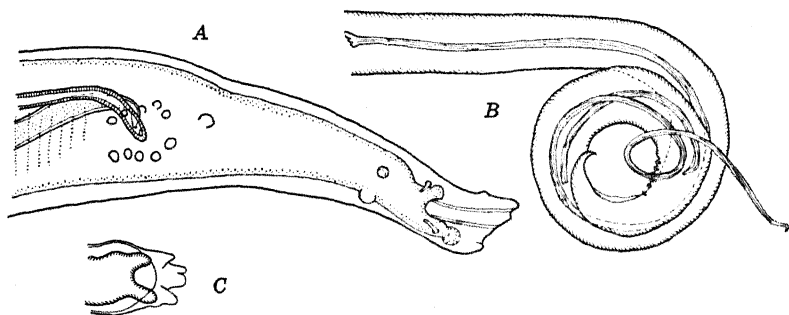


FIG. 143. *D. perstans*: A, posterior end of ♂, ventral view (large spicule cut off at level of cloaca); B, same, lateral view; C, tip of tail of ♀. (After Chabaud, *Ann. parasitol. hum. et comp.*, 27, 1952.)

rain forests of west and central Africa. The incidence of infection increases with age, and in some areas in Congo, Uganda, and Cameroons practically all elderly people show microfilariae in the blood. It has also become established in northern South America and northern Argentina. The microfilariae (Fig. 138D) exhibit no periodicity. The thread-like adults live in deep connective tissue; the males are about 35 to 45 mm. long and only 60 μ in diameter, and the females 70 to 80 mm. and 120 μ in diameter.

The infection seems to produce no evident symptoms, at least in the majority of cases, but Enzer observed cases of persistent headache and drowsiness in individuals whose blood was teeming with the embryos and in whom there was no other evident cause for the symptoms.

Others have observed continuous fever. Sharp (1928) showed that the intermediate hosts in the Cameroons are minute nocturnal midges, *Culicoides austeni* and *C. grahami* (see p. 658). Chardome and Peel (1949) found that *Culicoides grahami* readily ingested skin-inhabiting microfilariae of *Dipetalonema streptocerca* (see below) but not those of *D. perstans* and questioned *Culicoides* being a vector of *perstans*, but later work in British Cameroons confirmed Sharp's work (see p. 658). Development takes place in the breast muscles of the flies, and infective larvae invade the head in about 8 or 9 days. Since the vectors are very numerous but only harbor a few infective larvae, there is a high incidence of light infections, whereas in *Loa* infections (see above) unevenly distributed but heavier infections are the rule. This is because the *Chrysops* vectors are less abundant, but one fly may harbor hundreds of infective larvae.

There are contradictory reports on the effectiveness of Hetrazan in eliminating the microfilariae of *D. perstans*; possibly this varies with the location of the adult worms.

Another species of *Dipetalonema*, *D. streptocerca*, was long known only by the microfilariae (see p. 463), which resemble those of *D. perstans* but are usually longer and more slender and are found in the skin like those of *Onchocerca*. It occurs in 2 to 100 per cent of natives in some parts of west and central Africa, and also occurs in apes. Only a few adults of this species have been found. No symptoms can definitely be ascribed to it. Similar larvae were found in six of eleven chimpanzees in Belgium Congo; the adult worms were located in connective tissue. The intermediate host was shown by Chardome and Peel (1949) to be *Culicoides grahami*.

Mansonella ozzardi

This worm, related to *Dipetalonema perstans*, is common in parts of the West Indies, Yucatan, Panama, and neighboring coasts of South America; it is also present in 25 to 30 per cent of the people in northern Argentina. The adults, found in the mesenteries or visceral fat, are about the size of *Wuchereria bancrofti*; the females are characterized by a pair of flap-like processes with fleshy cores at either side of the tail. Only a single incomplete male has even been found. The microfilariae (see p. 463 and Fig. 138E) are much like those of *D. perstans* but differ in having pointed tails without nuclei. There is no evidence that the worm is pathogenic. Buckley (1934) showed that the intermediate host in St. Vincent, W. I., is *Culicoides furens* (see p. 658), the development being similar to that of *D. perstans*; it is completed in about 7 or 8 days.

Onchocerca

The members of the genus *Onchocerca* are long, thread-like filarial worms which live in the subcutaneous and connective tissues of their hosts, where they are usually imprisoned in tough fibrous cysts or nodules. The females are so extremely long and hopelessly tangled that it is very difficult to get entire specimens. In man the females sometimes reach a length of 500 to 700 mm. (over 2 ft.), and in cattle twice this length or even more, with the diameter of a coarse sewing

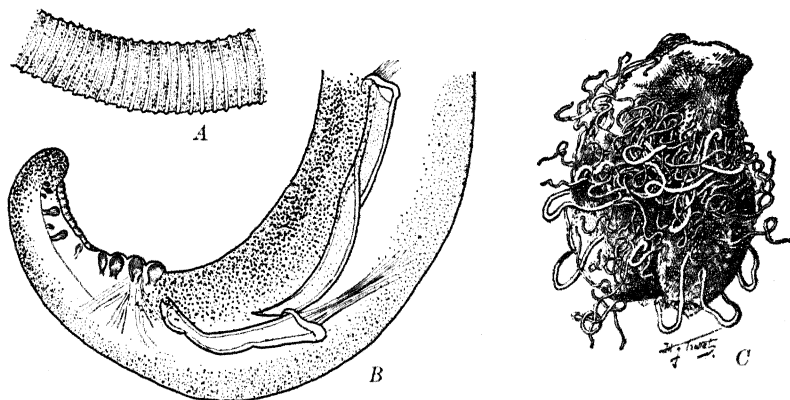


FIG. 144. *Onchocerca volvulus*: A, portion of body showing annular thickenings; B, tail of male, showing spicules and papillae; C, an opened *Onchocerca* nodule showing tangled worms inside. $\times 2$. (A and B adapted from Fülleborn, in Kolle u. Wassermann, *Handbuch der path. Mikro-org.*, Vol. 6, 1929. C, after Brumpt, *Précis de parasitologie*, 1949.)

thread (about 0.3 to 0.4 mm.). The males are very small by comparison, about 20 to 50 mm. long, with a diameter of 0.2 mm. The microfilariae (see p. 463 and Fig. 138F) are sharp-tailed and unsheathed, and differ in that they do not enter the blood stream but localize in the skin and eye tissues.

A number of species have been described from horses, cattle, antelopes, and man, but they are very difficult to distinguish, and some have been differentiated mainly on the basis of the usual location of the nodules in the host's body. All the species are recognizable by the presence of thickened ridge-like rings on the cuticle (Fig. 144A), much more conspicuous in females than in males. The male has a coiled tail bluntly rounded at the tip and provided with papillae but no alae (Fig. 144B); there are two unequal spicules. The females have the vulva near the end of the esophagus and have a bluntly rounded tail.

Some species, especially *Onchocerca gibsoni*, injure the hides and

carcasses of cattle by the hard nodules that form. Another, *O. reticulata* (= *cervicalis*), inhabits the neck ligament of horses, causing "poll ill" and fistulous withers; the microfilariae cause papular, itching skin sores. This species occurs in the United States. The intermediate hosts of these species of *Onchocerca* of horses and cattle are species of *Culicoides* (see p. 659). This may also be true of *O. armillatus*, which causes aneurysms in the aorta of cattle in Africa.

ONCHOCERCA VOLVULUS

Human onchocerciasis is caused by *O. volvulus*, which occurs in southern Mexico, Guatemala, Salvador, and northwest Venezuela in the Western Hemisphere, and in central Africa in the Old World. It was probably originally an African infection introduced rather recently into Central America, where it was not discovered until 1915. In some localities 80 to 100 per cent of the people harbor this worm, and 5 per cent of them lose their sight.

Life Cycle. The developing worms creep about in the subcutaneous tissue, but when they come to rest there is an inflammatory reaction which results in the formation of the characteristic fibrous cysts; in one instance a nodule was found in a child 2 months old, but usually a somewhat longer time is required for them to appear. They may grow to a diameter of 1 cm. in a year, but usually the growth is slower. Strong et al. in Guatemala usually found 3 or 4 worms in a nodule, but in Africa there are composite nodules containing more than 100 worms. The worms lie in tangles in the cysts (Fig. 144C), which vary from the size of a pea or smaller to that of a pigeon's egg; usually a swarm of microfilariae is present also. In most localities infected people have only one to half a dozen nodules, but in some places in Africa 25 to 100 nodules are commonly seen, most of them only a few millimeters in diameter. There is ample evidence, however, that not all of the adult worms become encapsulated. The adults are long-lived; in Kenya microfilariae were still present in the blood seven years after reinfection was stopped by eradication of the intermediate host.

The microfilariae, 250 to 360 μ long and unsheathed (Fig. 138F), escape readily from the prisons which enclose their parents and make their way, not into the blood stream, but into the connective tissue just under the skin, where they accumulate in large numbers. Sometimes they emerge by hundreds when a bit of excised skin is placed in a saline solution for two or three hours.

The intermediate host in Africa was shown by Blacklock in 1926 to be a species of blackfly, *Simulium damnosum* (see p. 664); *S. neavei* is also a vector in Belgian Congo and Kenya. In Guatemala and

Mexico *S. ochraceum* seems to be the only really anthropophilic species, and onchocerciasis is common only where this species is present; but *S. metallicum* also bites man, and *S. callidum* does so to a less extent. Several other species may be locally important. The microfilariae of *Onchocerca* are seldom found below the knee, where *S. metallicum* and some other species usually bite. It has been suggested that the *Onchocerca* infections often found in wild-caught specimens of *metallicum* may represent *O. gutturosa* of cattle or *O. reticulata* of horses, which are also present. However, as far as is known, the latter species, and perhaps some of the cattle species also, are transmitted by *Culicoides* (see p. 659).

When the fly is biting, its salivary secretions attract the microfilariae from adjacent areas of skin so that even 100 to 200 may be ingested in a single meal. Rapid development takes place in the thoracic muscles; infective larvae are produced in 6 to 7 days, according to Wanson (1950).

Epidemiology. In central Africa the infection has a wide distribution, largely coinciding with that of *Simulium damnosum* and *S. neavei*, but in America it is mostly limited to a narrow strip on the Pacific slope in Guatemala and southwestern Mexico, between about 2000 and 4500 ft. elevation, where coffee is extensively grown, and where there are numerous small, shaded, trickling streams arising from springs, in which *S. ochraceum* breeds.

In Mexico 20,000 people are affected in Chiapas and 11,000 in Oaxaca, but apparently the infection has not yet spread over all the areas where it could thrive. Dampf (1942) called attention to the danger of its spread along the Pan-American Highway, which passes through foci in both Mexico and Guatemala. The danger is greatest to natives since, as in the case of *Wuchereria bancrofti*, harmful effects develop only after continued exposure to infection.

Pathology. As already noted, the outstanding feature of onchocerciasis is the development of fibrous nodules enclosing the worms (Fig. 144C). In parts of Africa the nodules are largely confined to the trunk, especially just over the hips and on the knees, elbows, ribs, etc., but in some regions of the Belgian Congo, and especially in Central America, they are commonly found on the head. In Guatemala about 95 per cent are on the head, especially about the ears. The location of the nodules seems to be influenced by pressure on the skin, either by bones or by hats or clothing, which might temporarily make the going hard for the migrating worms and impede them long enough for the tissues to start the imprisoning process. The site of the bites of the intermediate hosts is certainly not the determining factor.

Ordinarily the nodules are not painful, and seldom suppurate, so usually give very little trouble. The microfilariae, however, which creep in the skin, not necessarily in the immediate vicinity of the nodules, cause other disturbances. In Africa, onchocerciasis is commonly associated with a peculiar thickened, scaly, lizard-like skin, especially around the middle part of the body, but not on the head, whereas in Central America there are more likely to be erysipeloid rashes on the head (coastal erysipelis). A more marked difference between the infection in Africa and America is the degree of lymphoid involvement. In Africa enlarged lymph glands containing microfilariae, lymph scrotum, and elephantiasis of the scrotum and legs are frequently associated with *Onchocerca* infections, even where *Wuchereria bancrofti* is absent. The reasons for these differences have not been explained.

The most serious complication of the disease is interference with the eyes, often ending in blindness. This is very prevalent in the endemic zones of Guatemala and Mexico, where in some localities 10 to 25 per cent of the population suffer from partial or total blindness. This is also true in some places in Africa, although in some localities where the nodules are mainly on the trunk, eye disturbances are much less frequent.

Strong (1934) carefully investigated this condition in Guatemala and found that the embryos escaping from nodules on the head had a tendency to invade the tissues of the eye—conjunctiva, cornea, iris, and other parts, sometimes even the optic nerve. Eye disturbances usually occur among adults with a history of nodules extending over 4 or 5 years or more. The lesions are chronic and progressive, beginning with injection of the conjunctiva, inflammation of conjunctiva and cornea, and development of opaque spots which run together. These lesions are due partly to irritation set up by the continual passage of numerous embryos through the eye tissues, and probably in part to allergic irritation. After the corneal tissues of the eye have become opaque, complete restoration of sight is not possible, but there is often some degree of improvement, or at least arrest of further harm, after removal of nodules on the head or destruction of microfilariae by Hetrazan treatment.

Diagnosis. Diagnosis can usually be made by puncturing and aspirating a nodule, by excising a small piece of skin with a razor (preferably not deep enough to draw blood), or by applying a cover-slip to the blood-stained exudate pressed out after four or five superficial scratches with a sharp instrument. Skin from the shoulder region, around the umbilicus, or in the vicinity of nodules is likely to provide the largest number of microfilariae, regardless of the situation of the

nodules. Examination of fed blackflies (xenodiagnosis) may be an even better method when feasible. Precipitin and skin reactions to filarial antigens are unreliable, but a skin reaction following a single dose of Hetrazan is of diagnostic value.

Treatment. The most effective treatment is excision of the nodules, which is usually possible. By systematically doing this, the amount of infection has been markedly reduced in Mexico.

Only two drugs have thus far proved useful in treatment. One, Hetrazan (see p. 472), has spectacular effects on the microfilariae, completely destroying them in a few hours, but it has a slow and unreliable effect on the adult worms, so the microfilariae eventually return. The chief disadvantage is that the rapid destruction of the microfilariae commonly brings on severe allergic reactions—fever, joint pains, inflamed and itchy skin, enlarged lymph nodes, and irritation of the eyes. These symptoms reach their height in 12 to 15 hours, and may be severe enough so that the treatment is considered worse than the disease. Use of small doses to begin with, together with anti-histaminic drugs may alleviate this trouble. The recommended dosage is 2 mg. per kg. three times a day for 2 or 3 weeks, or 10 mg. per kg. once daily for 1 week, repeated every 6 months. The other drug is Suramin (Bayer 205), 1 gram each week for 5 weeks. This kills the adult worms; the microfilariae then gradually disappear in the course of several months, and the nodules shrink. But this drug is very toxic, produces severe reactions, and requires intravenous injection. Present indications are that Suramin treatment following Hetrazan may be a good procedure. Systematic "denodulization" is still the safest and best method of treatment.

Prevention. Among natives exposure to bites of blackflies is unavoidable. Systematically destroying the parasites or nodules in human beings in more or less circumscribed foci, as in Mexico and Guatemala, might be possible, but it is thought to be impracticable in Africa. Animals are not believed to constitute important reservoirs, since the parasites, though morphologically indistinguishable, seem to be biologically distinct.

A better alternative is elimination of breeding places of blackflies or treatment of them with larvicides (see p. 665), which has been done with remarkable success in Mexico and Guatemala, and also in areas in Africa.

Other Filariae in Man

Scattered cases of a number of other adult or immature filariae which are of doubtful nature or unknown affinities are on record. One im-

mature adult, *Filaria conjunctivae*, believed by Desportes (1939-1940) to belong to the genus *Dirofilaria*, has been found occasionally in cyst-like tumors of the eye, nose, arm, and mesentery in Europe and India. Two cases were recently reported by Faust et al. in Florida; they believe that these worms are *Dirofilaria immitis* which have lost their way in an abnormal host. No male specimens have been found. There are a few records of several other forms, most of them sexually immature, from the eye socket, lens, skin, or other places, which have not been definitely classified, and all of which are probably only accidental human parasites. One male of *Dirofilaria repens*, normally in the skin of dogs, was reported from a nodule in the eyelid of a woman in Russia. There is one record from Brazil of a filaria from the heart, *D. magalhaesi*, a worm closely related to the common heart filaria of the dog, and Faust in 1939 recorded a single male *Dirofilaria* from the inferior vena cava of an old Negress in New Orleans.

The possibility of larval filariae sometimes making their way to the human central nervous system and causing nervous disturbances has been pointed out by Innes and Shoho (1953), who showed that lesions in the brain, spinal cord, or eye of horses, sheep, and goats are due to invasion by larvae of species of *Setaria* (see below) in unnatural hosts; these lesions result in lumbar paralysis or, when in the eye, a disease called kumri. Whitlock (1952) found immature filariae of a new species, *Neurofilaria cornellensis*, in the central nervous system of sheep in New York State suffering from a similar disease.

Filariae in Domestic Animals

Except for *Onchocerca* infections in cattle and horses (see pp. 477-478) and occasional injury to horses from *Onchocerca* infections in the neck ligament, larger domestic animals suffer relatively little from filarial infections. *Setaria equina* and *S. labiato-papillosa* are often found in the peritoneal cavities of horses and cattle, respectively, but do no appreciable damage except when, during an early period of wandering through the tissues in abnormal hosts, they enter the eye or central nervous system (see preceding paragraph). Innes (1953) quotes a Korean report which states that mosquitoes (*Anopheles sinensis*, *Armigeres obturbans*, and *Aedes togoi*) are transmitters, but *Stomoxys* is said to transmit the cattle species. In the central and western states another species, *Stephanofilaria stilesi*, causes skin sores in cattle and sometimes in goats and pigs; in India *S. assamensis* causes "hump sore" in cattle, and sometimes ulcers in the ears. It is a small worm, the females only 6 to 8 mm. and the males 2 to 3 mm. long, with cuticular spines behind the mouth.

In the Old World horses are afflicted by *Parafilaria multipapillosa*, and cattle by *P. bovicola*; the females are 40 to 70 mm. long and the males about 30 mm. As in the genus *Filaria* the vulva opens just beside the mouth. These worms live in subcutaneous tissue and pierce the skin to deposit their embryonated eggs, causing "summer bleeding"

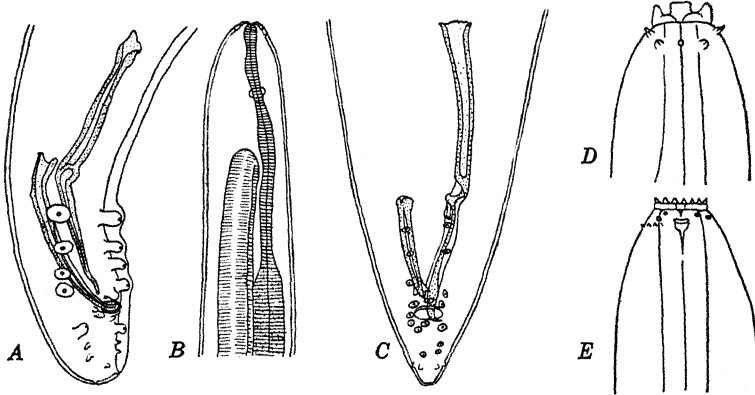


FIG. 145. Filariae of animals. A, *Dirofilaria immitis* of dogs, posterior end of ♂; B, same, anterior end of ♀; C, *Setaria equina*, posterior end of ♂; D, same, anterior end; E, *Stephanofilaria*, anterior end. (A–C, after Mönnig, *Veterinary Helminthology and Entomology*, Williams and Wilkins. D and E after Whitlock, *Practical Identification of Endoparasites for Veterinarians*, Burgess.)

from small nodules, and injuring the hides. Muscoid flies feeding on the blood suck up the eggs and serve as intermediate hosts. Sheep suffer from sores on the head caused by *Elaeophora schneideri*, the adult of which lives in the carotid and iliac arteries.

Heartworm of Dogs (*Dirofilaria immitis*). Dogs suffer severely from this worm, which usually inhabits the right ventricle of the heart and the adjacent parts of the pulmonary arteries. The females are 20 to 30 cm. long, the males about 12 to 18 cm. The microfilariae are unsheathed and show a partial periodicity. The infection is found in all warm climates and is very common in southern United States, but heavy infections are limited to coastal areas. Various mosquitoes, especially certain species of *Aedes*, are intermediate hosts, and fleas may also serve as vectors. The heavy infections near the coast are possibly due to salt-marsh mosquitoes serving as vectors. Development takes place in the Malpighian tubules of mosquitoes, but in the hemocoel of fleas.

The adult worms usually remain in the right ventricle, but may spread into the pulmonary arteries when excessive numbers are present.

Pulmonary circulation is interfered with, and dogs with fifty or more worms cough, and quickly show respiratory difficulties on exercise, or may collapse entirely. Treatment with antimony compounds, especially Fuadin, kills the microfilariae and eventually kills or sterilizes the adults. Arsenamide kills the worms but has little or no effect on the microfilariae. Hetrazan quickly kills the microfilariae, but its effect on adult worms is questionable. Since dead worms tend to enter and clog the pulmonary arteries, exercise should be reduced to a minimum during and for two months after treatment.

SUBORDER SPIRURATA

II. SPIRUROIDS (SUPERFAMILY SPIRUROIDEA)

Morphology. The superfamily Spiruroidea contains a large number of worms that are parasitic in all kinds of vertebrates. They vary enormously in form and include slender, filaria-like worms such as *Thelazia* and *Gongylonema*; large heavy-bodied forms superficially resembling ascarids, such as *Physaloptera*; short, thick forms such as *Gnathostoma*; and forms with bizarre females nearly spherical in shape, such as *Tetrameres*. Some have the head or body armed with spines or other cuticular embellishments. The mouth opens into a chitinated vestibule; in some, e.g., *Thelazia* (Fig. 146B), it has no lips, but in the majority there is either a single pair of lateral lips, e.g., *Physaloptera* and *Gnathostoma* (Fig. 146C, D), or a pair of dorsoventral lips in addition to the lateral pair, but never three or six lips. The vulva usually opens in the middle region of the body, but near the anus in *Gongylonema*. In the males the tail is spirally coiled; it usually has broad alae often ornamented with cuticular markings and provided with pedunculated papillae.

Important Species. The accompanying table gives a list of the forms that are of interest as parasites of domestic animals, including those that are accidental parasites of man. It will be seen that, though some of them live in the alimentary canal, most of them live in its walls or in more distant parts of the body.

Life Cycles. Except for *Thelazia* and specimens of *Spirocerca* that get misplaced in aortic cysts, the eggs of all these spiruroids get access to the alimentary canal and are voided with the feces. In all cases in which the life cycles have been worked out, except *Thelazia*, the thick-shelled, embryonated eggs are swallowed by arthropods either in soil or in water, and in these the larvae develop. In most cases infection of the final host results from the swallowing of the intermediate host, but in at least some of the species accessory methods of transfer have been evolved. Although the species of *Habronema* of horses, which

SPIRUROIDS OF INTEREST AS PARASITES OF DOMESTIC
ANIMALS. ACCIDENTAL PARASITES OF MAN MARKED " * "

Name of Parasite	Definitive Hosts	Habitat	Intermediate Hosts
<i>Ascarops (Arduenna)</i> and <i>Physocephalus</i> <i>Cheilospirura</i> spp.*	Pigs Chickens and turkeys	Stomach Walls of gizzard	Dung beetles Grasshoppers, sow bugs (also beetles and sandhoppers)
<i>Echinuria</i> spp.	Ducks and geese	Stomach and small intestine	<i>Daphnia</i> , amphipods
<i>Gnathostoma spinigerum</i> *	Fish-eating carnivores	Stomach tumors	First host: <i>Cyclops</i> ; second: fish, frogs, or snakes
<i>Gongylonema</i> spp.*	Ruminants, pigs, horses, rodents, fowls	Walls of esophagus or rumen	Dung beetles or roaches
<i>Habronema microstoma</i> , <i>muscae</i> and <i>macrostoma</i>	Horses	Mucosa or lumen of stomach	Maggots of <i>Stomoxys</i> or <i>Musca</i> (escape from proboscis of adults)
<i>Hartertia gallinarum</i> <i>Physaloptera</i> spp.*	Chicken (Africa) Insectivorous and carnivorous mammals, birds, reptiles (common sp. in opossum)	Small intestine Stomach or intestine	Workers of termites Cockroaches, earwigs, beetles, and crickets
<i>Protospirura</i> spp.	Rodents, monkeys, etc.	Esophagus and stomach	Roaches, fleas?
<i>Spirocerca sanguinolenta</i>	Dogs	Tumors on esophagus, stomach, or aorta	Dung beetles
<i>Tetrameres</i> spp.	Poultry	Glands of proventriculus	Grasshoppers, roaches, amphipods, <i>Daphnia</i>
<i>Thelazia callipaeda</i> *, <i>rhodesi</i> and <i>californiensis</i> *	Ruminants, dogs and man	Eye	<i>Musca</i> spp.
<i>Oxyspirura mansonii</i>	Chicken	Eye	Roaches

develop in maggots of stableflies or houseflies, may infect their hosts through the swallowing of infected adult flies, the larvae, after development in the Malpighian tubules or fat bodies, make their way to the head and voluntarily escape from the labium on warm wet surfaces as do filariae. They thus reach the lips, nose, or wounds, and finally infect

via the mouth when licked off and swallowed. Although apparently unable to reach their destination by burrowing into the skin, it is obvious that their life cycle is a step toward the filarial type. *Thelazia* larvae also escape from the proboscis of flies feeding around the eyes, thus reaching their destination directly.

Infective spiruroid larvae if eaten by abnormal hosts may burrow into the tissues and become re-encapsulated. The writer found armadillos from hog lots with hundreds of cysts containing dead larval stomach-worms of pigs (*Ascarops* and *Physocephalus*) obtained from eating infected grubs before the pigs got them. For *Gnathostoma* this seems to be routine procedure, for whereas cats are easily infected by feeding them gnathostome larvae encysted in second intermediate hosts (fish, frogs, snakes), attempts to infect them by feeding infected *Cyclops* have so far failed.

Since a considerable number of spiruroids are capable of partial and sometimes complete development in human beings, it is obvious that we owe our relative immunity to spiruroid infections to the fact that we are not for the most part voluntarily insectivorous. In the following paragraphs are considered briefly the principal forms recorded from man.

***Gongylonema*.** These slender, filaria-like worms (Fig. 146A) live in the walls of the esophagus or mouth cavity. The females reach a length of 15 cm. and the males 6 cm., but the diameter is only 0.2 to 0.5 mm. Eight rows of wart-like bosses on the anterior end are a characteristic feature; the vulva of the female is not far from the anus, and the male has very unequal spicules and a coiled tail with asymmetrical alae.

Only sixteen human infections have been recorded, all of them with immature worms; although given the name *Gongylonema hominis*, they are probably identical with *G. pulchrum* of pigs and ruminants. Several cases occurred in southern United States. All the patients were aware of the active migrations of the worms under the lips or cheeks and were much annoyed by them; the worms move so rapidly that considerable dexterity is required to remove them. Two of the patients also had nervous disorders which disappeared after they got rid of their parasites. Since dung beetles and roaches are the intermediate hosts it is obvious that human infection could not be common, for our appetites tend in other directions.

It is of interest to note that two species in rats, *G. neoplasticum* and *G. orientale*, frequently stimulate cancerous growths, but there is no evidence that other species do so.

***Physaloptera*.** The genus *Physaloptera* contains numerous species parasitic in all sorts of carnivorous and insectivorous land vertebrates.

They are large worms (Fig. 146D), superficially resembling ascarids; they live most frequently in the stomach but may also live in the intestine and occasionally even the liver; they bury their heads in the mucous membranes and cause sores and ulcerations. The females are usually 3 to 10 cm. long by 1.2 to 2.8 mm. in diameter; the males about half this size. A characteristic feature is a collarette surrounding the head end and a pair of trilobed lips. The vulva is anterior in position. The male has a coiled tail with broad asymmetrical alae which meet in front of the anus and have very long papillae; the spicules are very unequal. One species, *P. caucasica*, normally parasitic in African monkeys, is said by Leiper (1911) to be fairly common in natives of tropical Africa; one case was found in the Caucasus in Europe.

***Protospirura muricola*.** Though not yet recorded from man, this rodent parasite has been reported by Foster (1938) as causing an injurious and often fatal infection of captive monkeys. In general appearance it resembles a small *Physaloptera* but lacks the collarette. The parasites block the esophagus and irritate the stomach wall, sometimes perforating it. Cockroaches serve as intermediate hosts. It becomes more and more evident that eating roaches is a very bad habit for the animals that habitually indulge in it.

***Gnathostoma spinigerum*.** This is a very robust worm, 25 to 50 mm. long, with a globular swelling at the head end which is armed with eight or more rows of thorn-like hooks (Fig. 146C). The mouth is bounded by a pair of fleshy lateral lips. Behind the swollen head the body is clothed with overlapping rows of toothed scales, which gradually dwindle away near the middle of the body.

The natural hosts of this species are wild and domestic cats and less frequently dogs. The adults inhabit large tumors, sometimes an inch in diameter, in the stomach wall, which open into the stomach by one or more pores. Other species in the Orient occur in the stomach of pigs, and one, *G. nipponicum*, in esophageal tumors in a very high percentage of mink in Japan. In the United States *G. spinigerum* has been reported rarely from cats; other species occur in raccoons and opossums.

The stomach tumors may cause fatal peritonitis when, as sometimes happens, they open into the body cavity. The seasonal occurrence of the parasites in cats, as seen by the writer in Calcutta, suggests that they may very commonly be fatal, for it seems impossible that the tumors could disappear completely soon after the worms had left.

In 1925 the writer found a high percentage of snakes near Calcutta to harbor larvae of *Gnathostoma*, which, when fed to cats, developed first in the liver and subsequently invaded the stomach wall. Later

Prommas and Daengsvang (1933) showed that *Cyclops* served as first intermediate hosts, and a few years later it was shown that when infected *Cyclops* are swallowed by fishes, amphibians, or snakes the larvae escape, invade the tissues, and become re-encysted in the flesh of these second intermediate hosts. Carnivores become infected when they

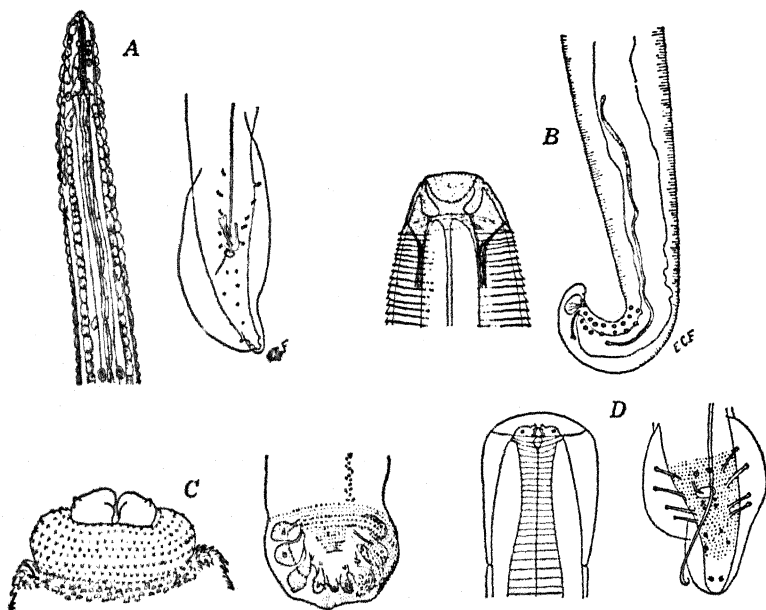


FIG. 146. Heads and tails of male spiruroid worms found in man. A, *Gongylonema pulchrum*; head, $\times 45$; tail, $\times 48$. B, *Thelazia callipaeda*; head, $\times 210$; tail, $\times 33$. C, *Gnathostoma spinigerum*; head and tail, $\times 39$. D, *Physaloptera caucasica*; head, $\times 22$; tail, $\times 16$. (A, B, and D after various authors, adapted from *Human Helminthology*, by Ernest Carroll Faust, Lea and Febiger, Philadelphia. C from Yorke and Maplestone, *Nematode Parasites of Vertebrates*.)

eat these hosts, but not when fed *Cyclops*. In Thailand 92 per cent of frogs, 80 per cent of eels, and 30 to 37 per cent of certain other food fishes in the markets were found to harbor larval gnathostomes. In southern Japan Miyazaki (1954) reported finding larvae in about 60 to 100 per cent of a fresh-water fish, *Ophicephalus argus*, in some parts; this fish is commonly eaten raw by the Japanese.

When ingested by man, *Gnathostoma spinigerum* larvae develop to morphologically mature worms, but remain sexually immature. Like many other helminths in a strange host, they fail to find their way to their proper destination, in this case the stomach wall. Instead they

wander aimlessly in the body, usually in or under the skin, but sometimes in the mucous membranes or viscera. Occasionally they blunder into the eye or even the brain. During their wanderings they most commonly cause migrating but intermittent swellings or edema, but sometimes a creeping eruption. Eventually they usually become encapsulated or escape through an abscess.

Human gnathostome infections have long been known to be of frequent occurrence in southeast Asia, especially in Thailand. The writer found eggs of the worm in presumably human feces on two occasions in Burma, so it is possible that the worm does occasionally mature in the human stomach. Since the end of World War II edema or creeping eruption caused by *G. spinigerum* was found by Miyazaki (1954) to be very common in southern Japan. In one report over one-third of 3900 patients examined were found infected. A single infection with a gnathostome of pigs, probably *G. doloresi*, has been reported from a man in Tokyo.

***Thelazia* spp.** These slender little worms, possibly more nearly related to the filariae than to the spiruroids, inhabit the conjunctival sac and lachrymal ducts of animals and occasionally man. At times they creep out over the eyeball, later returning to their nest in the inner corner of the eye. *T. callipaeda*, primarily a parasite of dogs in India, Burma, and China, has been reported from man four times in China. *T. californiensis*, reported by Stewart from sheep, deer, and dogs in brushy, mountainous places in California, has been found in man twice. Other species are important parasites of the eyes of cattle and horses in some places; altogether nineteen species have been described from various mammals and birds.

The female worms are 7 to 19 mm. long, the males somewhat smaller. The cuticle is pleated into well-defined striations with sharp edges; there are no lips, but there is a short vestibule (Fig. 146B). The vulva is anterior as in filariae, and the male has no caudal alae. Krastin (1950) showed that certain flies of the genus *Musca* which cluster around the eyes of cattle serve as intermediate hosts for *T. rhodesi*, which is harbored by over 90 per cent of cattle in late summer in parts of eastern Siberia.

By their movements the worms irritate the eye considerably, causing a free flow of tears and injection of blood vessels, and sometimes severe pain and nervous symptoms. At first the eye is not seriously affected, but Faust (1928) observed that in the course of time the repeated scratching of the surface of the eyeball by the serrated cuticle of the worm causes the formation of scar tissue, and the eye gradually develops a cloudiness, progressing outward from the worm nest, which ultimately

reduces the vision. Cattle are sometimes blinded by a *Thelazia* in Africa and Asia.

After the eye is desensitized with 1 per cent cocaine, the worms are easily removed with a forceps or swab if seen, but several examinations are usually necessary in order to get a complete catch.

Cheilospirurua sp. Africa and Garcia (1936) found a specimen belonging to this genus in a nodule on the conjunctiva of a Filipino. Members of this genus, so far as known, normally live under the lining of the gizzard of birds. It is another example of abnormal behavior in an abnormal host.

SUBORDER CAMALLANATA. GUINEA WORMS (SUPERFAMILY DRACUNCULOIDEA)

The superfamily Dracunculoidea, placed by Chitwood in the suborder Camallanata, was formerly included with the filarial worms. It contains several genera of worms that are peculiar in the relatively enormous length of the female worms as compared with the midget males, and in the fact that during the course of their development the alimentary canal and vulva atrophy, leaving the body of the adult almost entirely occupied by the embryo-filled uterus. The embryos are liberated by the bursting of a loop of the uterus prolapsed through the mouth or through a rupture of the anterior end of the body. One genus, *Philometra*, contains parasites of the body cavity of fishes; the others, *Dracunculus*, *Aviosepiens*, and *Micropleura*, contain parasites of the connective tissues of mesenteries of reptiles, birds, and mammals. The guinea worm, *Dracunculus medinensis*, is a common human parasite in parts of Asia and Africa. Another species, *D. insignis*, is a parasite of raccoons in America, and occurs sporadically in mink, dogs, etc. The writer (1942) found *D. insignis* to be very common in the hind feet of raccoons in eastern Texas. The females closely resemble the human guinea worm of the Old World except for their smaller size (up to 16 in. long), but there are minor differences in the males. This species may be able to infect man, but no proved cases are known. In the Old World guinea worm infections only rarely occur in animals, although dogs and other carnivores are susceptible.

Dracunculus medinensis

Occurrence and Distribution. The guinea worm, *Dracunculus medinensis* (meaning the little dragon of Medina), has been known since remote antiquity, for one of its main strongholds is in the region of western Asia which cradled civilization. The "fiery serpents" which molested the Israelites by the Red Sea were probably guinea worms.

It is still, as it was in ancient times, one of the important scourges of life from central India to Arabia, and it is locally important in the East Indies, Egypt, and central Africa. Stoll (1947) estimated that there are 48,000,000 human guinea-worm infections in the world. The disease is commonly associated with dry climates because of the concentration of water supplies in step-wells or reservoirs and the greater opportunity for *Cyclops* in the drinking-water supply to become contaminated from human skin. In innumerable villages in central and western India up to 25 per cent or more of the population suffer annually from guinea-worm infections. The human guinea worm became established in a few localities in tropical America but seems to have died out.

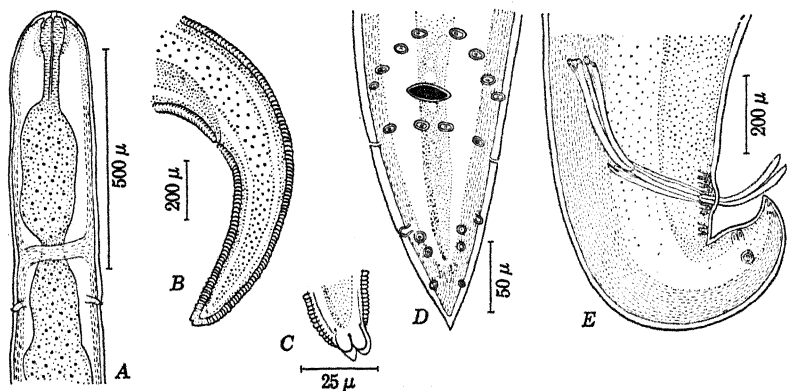


FIG. 147. *Dracunculus medinensis*, guinea worm. A, anterior end of ♂; B, posterior end of immature ♀; C, tip of tail of immature ♀, showing four processes (mucrones); D, tail of ♂, ventral view; E, tail of ♂, lateral view. (After Moorthy, *Parasitol.*, 23, 1937.)

Morphology. The gravid female worm, long the only form known, lives in the deeper layers of the subcutaneous tissues, where she usually can be seen lying in loose coils, like a small varicose vein, under the skin. Sometimes she is more easily felt than seen until she produces a skin ulcer through which she gives birth to myriads of embryos. She reaches a length of 2.5 to 4 ft. with a diameter of 1 to 1.5 mm. The head end is bluntly rounded, and commonly ruptured in worms which have begun expelling embryos. The tail is attenuated and sharply hooked.

The males were practically unknown until Moorthy and Sweet (1936) obtained them in experimentally infected dogs. Mature specimens measured 20 to 29 mm. in length and were found 15 to 20 weeks after infection, but were not found when the gravid females were found

in the skin at the end of 15 months. Males and young females of similar size (Fig. 147) have the simple mouth surrounded by papillae and have an esophagus about 10 mm. long; in the females the vulva is a little anterior to the middle of the body. The males have a spirally coiled tail with four pairs of preanal and six of postanal papillae, but no alae, and two nearly equal spicules 0.5 to 0.7 mm. long.

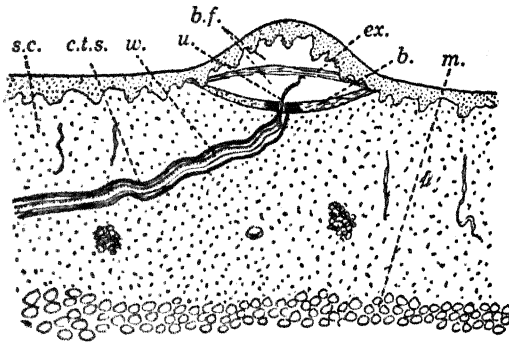


FIG. 148. Diagram of guinea worm in the skin at the time of blister formation; *b.*, base of ulcer; *b.f.*, blister fluid; *c.t.s.*, connective tissue sheath of worm; *ex.*, layer of exudate; *m.*, muscle layer; *s.c.*, subcutaneous tissue; *u.*, extruded uterus of worm; *w.*, worm. (Adapted from Fairley.)

Life Cycle. When ready to bring forth her young, the guinea worm is instinctively attracted to the skin, especially to such parts as are likely to, or frequently do, come in contact with cold water, such as the arms of women who wash clothes at a river's brink or the legs and backs of water carriers. The worm pierces the lower layers of the skin with the front end of her body and excretes a toxic substance that irritates the tissues and causes a blister to form over the injured spot (Fig. 148). The blister eventually breaks, revealing a shallow ulcer, about as large as a dime, with a tiny hole in the center. When the ulcer is douched with water a milky fluid is exuded directly from the hole or from a very delicate, transparent projected structure which is a portion of the worm's uterus. This fluid is found to contain hordes of tiny coiled larvae with a length of about 600μ , one-third of which is occupied by the long filamentous tail (Fig. 149).

An hour or so later a new washing with cold water will bring forth a fresh ejection of larvae, and so on until the supply is exhausted, a little more of the uterus being extruded each time. After each ejection of the larvae the protruded portion of the uterus dries up, thus sealing in the unborn larvae and saving them for the next douching. This procedure, of course, increases the chances of some of the larvae finding

Cyclops-inhabited water. The whole process is one of the neatest adaptations in behavior in all the realm of biology, enabling a blind, unmeditative, burrowing worm to give her aquatic *Cyclops*-inhabiting offspring a fair chance in life even on a desert. She turns what would seem to be a hopeless handicap into an actual advantage.

When all the young have been deposited under the stimulus of contact with water the parent worm shrivels and dies and is soon absorbed by the tissues.

The embryo worms, safely deposited in water, unroll themselves and begin to swim about. They remain alive for several days but eventually perish unless swallowed by a *Cyclops* (Fig. 149). When this

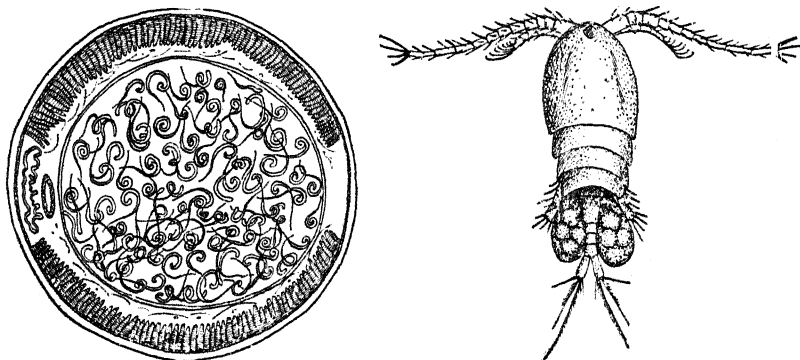


FIG. 149. Left, cross-section of guinea worm showing uterus filled with embryos, about $\times 30$ (after Leuckart). Right, a *Cyclops*, some species of which serve as intermediate hosts of guinea worm, about $\times 25$.

happens they burrow into the body cavity of the surprised *Cyclops*, reaching that destination in 1 to 6 hours. Moorthy never found a *Cyclops* with more than one larva in nature; when infected with more than four to five in the laboratory, development is interfered with. The writer never found more than two larvae of *Dracunculus insignis* to develop in experimentally infected *Cyclops*.

The larvae molt twice in the body cavity and reach the infective stage within 3 weeks. At this time they vary from 240 to 600 μ in length, the tail now being short. After feeding infected *Cyclops* to dogs the first specimens were found by Moorthy after about 10 weeks; they were deep in the connective tissues and only 12 to 24 mm. long, although the vaginas of females 24 mm. long already contained a mucoid plug, indicating that they had already been fertilized. The worms appear to come to maturity in about 11 to 12 months after infection.

Epidemiology. In western India the infection is always associated with step-wells which, instead of being provided with buckets and ropes, are approached by steps, the people standing foot- or knee-deep in the water while filling containers. During this time the parent worm ejects her offspring, and at the same time previously infected *Cyclops* are withdrawn with the water. In African villages, ponds function in a similar manner.

In an epidemiological study in the Deccan, India, almost no infection was found in children under 4, but after that the incidence increased steadily to 85 per cent in the 30- to 35-year age group, then gradually fell off again. There may be one to fifty worms per person but in most instances only one in a year. Few people suffer from infections for more than 4 years, after which immunity usually develops. The worms form their ulcers on the legs in about 90 per cent of cases.

Pathology. The first symptoms appear simultaneously with the beginning of the blister formation, and consists of urticaria, nausea and vomiting, diarrhea, asthma, giddiness, and fainting; some or all of these symptoms may be present. Fairley (1925) believes they are due to absorption of the toxin employed by the worm to form the blister. The symptoms strongly suggest an allergic reaction; injection of adrenalin brings about rapid improvement. Eosinophilia is marked.

Later symptoms result from secondary invasion of the ulcer by bacteria. The worms are usually mechanically extracted and, being elastic, are likely to break. The broken end of the worm draws back, carrying with it into its connective-tissue sheath various bacteria which produce abscesses. These may cause such severe infection as to necessitate amputation or may even lead to fatal blood poisoning. Joints are frequently involved, leading to permanent deformities. These occur with deplorable frequency in villages of the Deccan in India. There is some evidence that reinfections do not occur while an adult worm is still in the body. Most victims are incapacitated for several weeks; fortunately only a minority suffer permanent deformities or more serious consequences.

Treatment. Most drugs used against guinea worms have proved to be of little or no value, often, in fact, harmful, since local applications by natives after the ulcer has formed succeed only in causing secondary infections. Elliott (1942) reported excellent results from intramuscular injection of Phenothiazine emulsified in olive oil into a number of places close to the worm. Two to four grams of Phenothiazine can be injected at a sitting, with repetitions at weekly intervals; more than two courses are rarely needed. It takes 5 to 7 days for the

drug to act; if a worm is being or is to be extracted, it is better to wait this long after injections.

Extraction of the worm by winding it out on a stick is a time-honored method which, with a few scientific refinements, is still widely used. Native medicine men extract the worm through the ulcer by repeatedly dousing its head with water and then winding it out a little at a time. Care must be taken not to pull hard enough to rupture the worm; a safe extraction takes 10 to 14 days. If the ulcer is carefully treated with antiseptics, the worm can be withdrawn a little faster by exposing a loop and pulling it from both ends. Natives in India apply to the wound a green powder made of neem leaves, together with a choice assortment of contaminating bacteria, and the unfortunate patient has to fight his battle with the bacteria instead of the relatively innocent worm. If he loses his leg or his life it is the will of the gods and no fault of the doctor. Another native method is to apply a cone-shaped piece of metal over the exposed part of the worm and suck it vigorously until a negative pressure is created sufficient to draw the tissue up into the cylinder. The tongue is then applied and the finger quickly substituted, and after a few minutes the worm may be found in the tube.

By the use of local anesthetics and aseptic precautions, mechanical extraction is usually successful, and complete healing may follow in less than a week, as contrasted with the usual month.

Prevention. Prevention of the infection would be extremely simple if it were not for the scruples of the natives, often of religious nature, as to where and how they obtain and use their water. In India wherever step-wells are replaced by other types which keep the legs or arms out of the water, guinea worm disappears. If the water were strained through muslin to remove *Cyclops*, guinea worm would disappear, but even this is objected to. However, education and governmental pressure eventually bring results, and many areas in India that have suffered from guinea worm for centuries have been freed in recent years by altering the wells. Moorthy has had some success in destroying *Cyclops* by treating wells with dilute copper sulfate and "perchloron," and he reports that a fish, *Barbus puckelli*, feeds on them voraciously, but he emphasizes that abolition of step-wells is the only permanent and foolproof method of control.

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Part III ARTHROPODS

• 22 •

Introduction to Arthropods

To the average person it is astonishing to learn that the insects and their allies, constituting the phylum Arthropoda, include probably more than four times as many species as all other animals combined. It is even more startling for egotistical humanity to realize that this is not the age of man but the age of insects, and that man is only beginning to dispute with insects first place in the procession of animal life in the world.

The Arthropoda are the most highly organized of invertebrate animals. Their nearest allies are the segmented worms or annelids, i.e., earthworms and leeches, but most of them show a great advance over their lowly cousins. Like the annelids they have a segmented type of body, though in some types, such as the mites, all the segments become secondarily confluent. Like the annelids, also, the arthropods are protected by an external skeleton which usually consists of a series of chitinous rings encircling the body. The most obvious distinguishing characteristic of the arthropods is the presence of jointed appendages in the form of legs, mouth parts, and antennae. Internally they are distinguished from other invertebrates in that the body cavity, so conspicuous in the annelids, has been entirely usurped by a great expansion and running together of blood vessels, so that a large blood-filled space called a hemocoel occupies the space of the usual body cavity or celom. Within this space are blood vessels and a so-called heart, which retained their individuality while the other vessels fused. These vessels are not closed, however, but open into the hemocoel at each end.

Classification

The phylum Arthropoda is divided by Comstock into thirteen classes, but only four of these concern us as human parasites or disease transmitters, namely, the Crustacea, the Arachnida, the Pentastomida, and the Hexapoda.

Crustacea. The Crustacea, including crayfish and water fleas, are primarily gill-breathing arthropods of the water. They are geologically of great antiquity, and among them are the most primitive of the typical arthropods. Their appendages are usually numerous and, taking the group as a whole, show a wonderful range of modifications for nearly every possible function.

The Crustacea include many parasites of aquatic animals, among them some very highly modified and bizarre forms. Most of the so-called fish lice belong to the subclass Copepoda, the North American forms of which were dealt with by Wilson (1902-1922). The Cirripedia (barnacles) also include some parasites, among them the remarkable *Sacculina*, a parasite of crabs, which ends up as an external reproductive sac with a network of roots that ramify through the entire body of the host. A number of isopods and at least one amphipod (whale louse) have also become parasites. The biology of these crustacean parasites is interestingly discussed by Baer (1952). Small crustaceans of the order Copepoda serve as intermediate hosts of several worms parasitic in man and animals, namely, certain species of *Cyclops* for the guinea worm and for *Gnathostoma spinigerum*; certain species of *Cyclops* and *Diaptomus* for the tapeworms *Dibothriocephalus* and *Spirometra*; and *Diaptomus* for *Hymenolepis lanceolata* of ducks. Crabs and crayfish (members of the order Decapoda) serve as second intermediate hosts for the lung flukes, *Paragonimus*.

Arachnida. The Arachnida, including spiders, scorpions, and mites, represent the terminus of a separate line of evolution. They probably had a common origin with the Crustacea, but they have become adapted to terrestrial life. The members of this class have four pairs of legs as adults, two pairs of mouth parts, and no antennae. The head and thorax are grown together, forming a cephalothorax, and in the ticks and many mites not even the abdomen remains as a distinct section. The Arachnida breathe by means of "book lungs," or may have a system of tracheae similar to those found in the insects and myriapods. Some of the small mites, however, lack both book lungs and tracheae and respire through the cuticle. Only one of the eight orders of Arachnida, the Acarina (mites and ticks), contains parasitic species; many of these are important disease vectors. Some of the Arachnida are very poisonous, including some scorpions and centipedes and certain spiders, especially the black widows, *Latrodectes*, and the skin-destroying *Loxoceles laeta* of Chile, Argentina, and Uruguay.

Pentastomida. The Pentastomida are degenerate worm-like creatures which in the adult stage have no appendages except two pairs of hooks near the mouth. If it were not for the larval forms, which

have two pairs of short legs, their affinities with the arthropods might be doubted. They were formerly included with the mites for want of a better way of disposing of them. They have no circulatory or respiratory organs. Like many of the parasitic worms, they undergo their larval development in intermediate hosts.

Hexapoda. The Hexapoda, or insects, represent the zenith of invertebrate life. They are primarily terrestrial arthropods which breathe by tracheae. Their appendages, however, are reduced to one pair of antennae (except in Protura, which have none), three pairs of mouth parts (one pair more or less fused together), three pairs of legs, and usually two pairs of wings if not secondarily lost. All insects are readily divisible into three parts, the head, the thorax, and the abdomen.

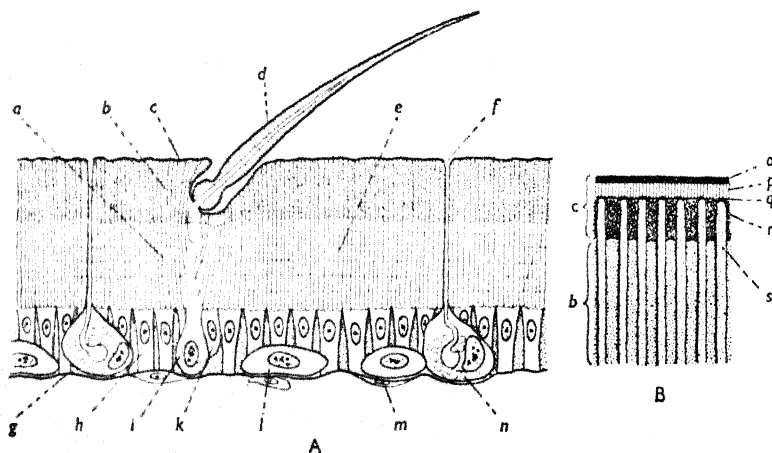


FIG. 150. A, section of typical insect cuticle; B, detail of epicuticle, schematic; a, laminated endocuticle; b, exocuticle; c, epicuticle; d, bristle; e, pore canals; f, duct of dermal gland; g, basement membrane; h, epidermal cell; i, trichogen cell; k, tormogen cell; l, oenocyte; m, haemocyte adherent to basement membrane; n, dermal gland; o, cement layer of epicuticle; p, wax layer; q, polyphenol layer; s, pore canal. (After Wigglesworth, *Biol. Revs.*, 23, 1948.)

Insect Morphology and Anatomy

The Cuticle. The cuticle of insects (Fig. 150) serves as an external supporting skeleton and as a place of attachment for muscles. It is a very complicated structure made up of an extremely thin outer layer of lipid material, the epicuticle (Fig. 150B), under which is a more or less thick layer composed of chitin and protein; in the outer portion of this, the exocuticle, the protein is tanned and hard, whereas in the deeper portion, the endocuticle, the chitin and untanned protein are

arranged in horizontal lamellae. Under the endocuticle is a single layer of epidermal cells. The exo- and endocuticle are provided with countless minute "pore canals," sometimes over 1,000,000 per sq. mm., which are believed to be filamentous cytoplasmic processes of the epidermal cells around which the cuticle was secreted.

The thin waxy layer of the epicuticle is responsible for the relative impermeability of the cuticle to water so that even insects with very soft skins can survive in dry places. Since the cuticle covers the fore and hindgut and the larger tracheae as well as the body surface, only the midgut is not plated with this moisture-conserving material. The insect cuticle is freely permeable by lipoid substances, which is of great importance in connection with such lipoid-soluble insecticides as the chlorinated hydrocarbons (DDT, etc., see p. 515) and their solvents.

Movement and expansion is allowed for by thin, lightly chitinized areas between rings or plates, except in the head and frequently the thorax. In the abdomen each ring has a dorsal plate or *tergite* and a ventral one or *sternite* (Figs. 193, 225). The thorax may also have lateral plates or *pleurites*. Since chitin is unaffected by alkalis, all the soft parts of insects may be dissolved away by treatment with potassium hydroxide, leaving all the cuticular characters, which are principally used in identifications, more easily examinable.

As arthropods grow they gradually become too large for their cuticles. The underlying hypodermis then lays down a new, thin, elastic cuticle under the old one. Certain cells produce a molting fluid which partially dissolves the old cuticle, making it easier to shed after a split has been formed in it. After the molt the new cuticle hardens and then gradually thickens again by formation of more chitin.

Mouth parts of Insects. Incredible as it may seem, the mouth parts of all kinds of insects, from the simple chewing organs of a grasshopper to the highly modified piercing organs of mosquitoes and the coiled sucking tube of butterflies and moths, are modifications of a single fundamental type which is represented in its simplest form in the chewing or biting type, as found in grasshoppers and beetles (Fig. 151). The mouth parts in these insects consist of an upper lip or *labrum*; a lower lip or *labium* bearing segmented appendages, the *labial palpi*; a pair of *mandibles* or jaws; a pair of *maxillae* lying ventral to the mandibles, bearing segmented *maxillary palpi*, and with two distal processes, the *galea* (lower in Fig. 151) and the *lacinia*; and the *hypopharynx* on the floor of the mouth, through which the ducts of the salivary glands open. In addition the roof of the pharynx, under the labrum, has a chitinized *epipharynx*; this is often combined with the labrum to form a *labrum-epipharynx*.

Legs. The legs of insects (Fig. 152A) consist of five parts: the coxa, trochanter, femur, tibia, and tarsus. The *coxa* articulates the leg with the body and sometimes appears more like a portion of the body than a segment of the leg. The *trochanter* is a very short inconspicuous segment and sometimes appears like a portion of the femur. The *femur* and *tibia* are long segments. The *tarsus*, or foot, consists of

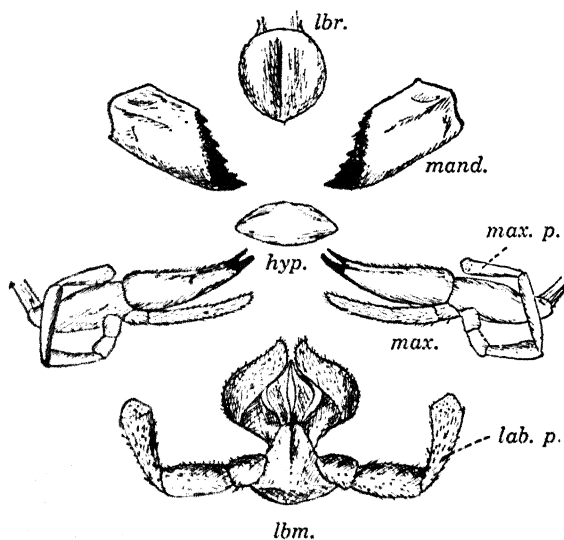


FIG. 151. Primitive mouth parts of a chewing insect; *lbr.*, labrum; *mand.*, mandible; *hyp.*, hypopharynx; *max.*, maxilla, consisting of a basal segment, the *stipes*, to which the maxillary palpus (*max.p.*) is articulated, and two distal parts, lateral *galea* and a mandible-like inner or medial lobe, the *lacinia* (black-tipped in figure); *lbm.*, labium, really a second pair of maxillae fused together, and bearing the labial palpi (*lab.p.*).

a series of segments, most commonly five; often the first segment is much the longest. Usually the tarsus is terminated by a pair of claws but sometimes only one. Often there are pad-like structures, *pulvilli*, which have glandular hairs or pores through which an adhesive substance is excreted, permitting the insects to walk on the under side of objects. Sometimes there is a pulvillus at the base of each claw and also a similar median structure between them, called an *empodium* (Fig. 152B).

Wings and Venation. The structure of the wings of insects is often of great use in classification and identification. Only in a few primitive orders are the wings primarily absent, although in many forms, especially parasitic ones, e.g., lice and fleas, they are secondarily

lost. Typically there are two pairs of wings, borne by the second and third segments of the thorax.

The wings originate as sac-like folds of the body wall, but the upper and lower surfaces become applied to each other and thus they appear as simple membranes. Where they flatten down against the tracheae the latter form hollow supports or *veins*. In most insects the majority

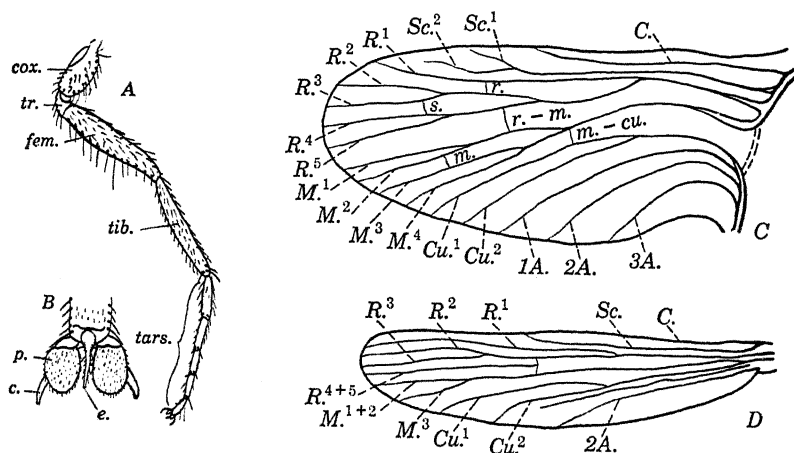


FIG. 152. Leg and wings of insects. A, leg; *cox.*, coxa; *fem.*, femur; *tars.*, tarsus; *tib.*, tibia; *tr.*, trochanter. B, foot, enlarged; *c.*, claw; *e.*, empodium; *p.*, pulvillus. C, diagram of primitive tracheae of wing from which the veins are derived. D, venation of a mosquito wing showing a comparatively simple modification; *c.*, costa; *Sc.*^{1 and 2}, subcosta, branches 1 and 2; *R.*^{1 to 5}, radius, branches 1 to 5; *M.*^{1 to 4}, media, branches 1 to 4; *Cu.*^{1 and 2}, cubitus, branches 1 and 2; *1A.*, *2A.*, and *3A.*, first to third anal; *r.*, radial cross vein; *s.*, sectorial cross vein; *r.-m.*, radio-medial cross vein; *m.*, medial cross vein; *m.-cu.*, medio-cubital cross vein (inadvertently omitted in mosquito wing). (A and B after Matheson, *Medical Entomology*, Comstock. C after Comstock, *Introduction to Entomology*, Comstock.)

of the veins are longitudinal, but there are usually a few cross-veins, which in some kinds of insects are very numerous. Figure 152C shows the hypothetical primitive arrangement of the venation of an insect wing, but in many insects the modifications brought about by coalescence, anastomosis, atrophy, and addition of extra branches and cross-veins often make it as difficult as a Chinese puzzle to determine the true homologies of the resulting veins. The spaces between the veins, called *cells*, are named after the longitudinal veins behind which they occur. Figure 152D shows the wing of a mosquito as an example of a comparatively simple modification.

Internal Anatomy. The alimentary canal of insects (Fig. 153) has three primary divisions which may be of very unequal extent, namely,

(1) the *foregut*, including pharynx, esophagus, crop, and proventriculus; (2) the *midgut*, including the stomach and sometimes a midintestine; and (3) the *hindgut*, including the small intestine and rectum. The foregut and hindgut are of ectodermal origin and are lined by cuticle; the midgut is endodermal. The junction of the midgut and hindgut is marked by the entrance of the *Malpighian tubules* (see second paragraph following).

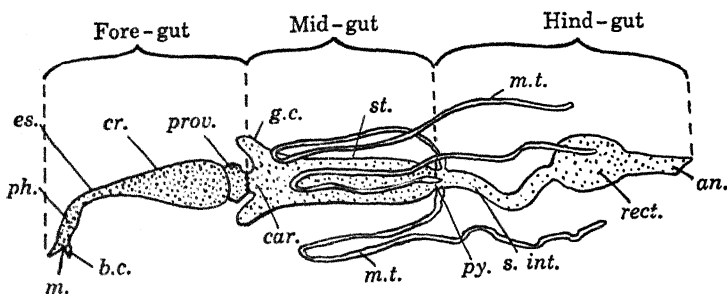


FIG. 153. Diagram of alimentary canal of an insect, showing portions pertaining to foregut, midgut, and hindgut, respectively; *an.*, anus; *b.c.*, buccal cavity; *car.*, cardium; *cr.*, crop; *es.*, esophagus; *g.c.*, gastric ceca; *m.*, mouth; *m.t.*, malpighian tubules; *ph.*, pharynx; *prov.*, proventriculus; *py.*, pylorus; *rect.*, rectum; *s.int.*, small intestine; *st.*, stomach. (Adapted from Snodgrass, *Principles of Insect Morphology*, McGraw-Hill.)

The *pharynx* in bloodsucking insects is muscular and acts like a suction pump. The ducts of the *salivary glands*, which themselves lie in the thorax, may open into the floor of the pharynx or in bloodsucking forms may unite and continue to the tip of an elongated hypopharynx. The pharynx is followed by an *esophagus*, which in some insects is expanded into a capacious *crop* and in some into a muscular *proventriculus* provided with chitinous teeth and serving the same function as the gizzard of a bird; in the mosquitoes three pouch-like *food reservoirs* are connected with the esophagus.

The true *stomach* follows the proventriculus and is sometimes provided with ceca that produce digestive juices; the stomach may constitute the entire midgut or it may be narrowed behind into a *mid-intestine*. The exposed cells of the midgut are protected in many insects by a delicate tubular membrane of cuticular material, the peritrophic membrane, secreted by cells in its anterior portion, but since this membrane lacks the epicuticular layer it is freely permeable. Enzymes may be liberated into the lumen either in vacuoles eliminated by the cells, or by disintegration of cells. The latter is important in the liberation of intracellular rickettsias into the lumen of lice. A number of

slender Malpighian tubules enter at the posterior end of the midgut. These function as excretory organs, corresponding to the kidneys of vertebrate animals; they extract waste products from the blood, convert them into insoluble form, and pass them into the hindgut, to be voided through the anus along with the feces.

The *hindgut* in some insects has a distinct *small intestine* followed by a more expanded *rectum*, but in others there is only a rectum, which is lined by chitin. Some insects have an expanded *anal pouch* at the posterior end.

The *tracheae* of insects constitute a ventilation system of air tubes ramifying all through the body even to the tips of the antennae and legs. They open by a series of pores along the sides known as *spiracles*.

The *nervous system* of insects is very highly developed. In some species the instincts simulate careful and accurate reasoning, and it is difficult not to fall into the error of looking upon them as animals endowed with a high degree of intelligence.

Sense Organs. *Sensory setae* which serve as organs of touch are widely distributed. Insects can detect extremely dilute odors over distances of probably a mile or more; they appear to depend more on the sense of smell than on any other type of sense perception.

The *compound eyes* of insects are less efficient than the eyes of vertebrates; their power of accommodation is limited, and insects can see distinctly only for short distances. The image produced by the thousands of facets is a mosaic one. Many insects also have simple eyes or *ocelli*. Many insects, at least those producing sounds, have organs of hearing, but often they are hard to recognize as such. They may be on the legs, antennae, or abdominal segments.

Reproductive Organs. The reproductive organs consist of paired ovaries or testes with their respective oviducts or sperm ducts opening near the posterior end of the abdomen, usually on the ventral side. All female insects have a *spermatheca* or storage sac for sperms, for most kinds of insects mate only once, whereas the egg-laying period may extend over a long time. In some insects, e.g., the fleas, the shape of the chitinized spermatheca is a good identification character. The eggs are fully formed with shells (chorion) before fertilization; one or more minute pores, the micropyles, permit entry of sperms, usually during passage through the vagina. Many insects have an *ovipositor* which may simulate a miniature saw, borer, or piercing organ for depositing the eggs; this versatile organ may be, in the Hymenoptera, modified into a *sting*. In the male the sperm ducts unite to form an *ejaculatory duct*, the terminal part of which may be chitinized and evaginated as an intromittent organ. Many male insects have highly

developed *external genitalia* in the form of *claspers* and accessory parts, details of which often provide valuable identification marks. Some species of *Culex* cannot be differentiated with certainty in any other way. (See Figs. 205 and 228.)

Life History

Most insects hatch from eggs deposited by the mother, but in some instances free young are born; in the Pupipara and in tsetse flies the eggs hatch before birth and the young are retained in the body of the mother until they are ready for pupation. In this case only a few young are produced, but most insects lay large numbers of eggs, some all at once, some in batches at intervals, and others individually at short intervals.

Three principal types of life history can be recognized among insects. In the primitive subclass Apterygota alone there occurs *direct development*, in which the newly hatched insect is nearly a miniature of its parent and merely increases in size. This is also true of some of the higher insects that are secondarily wingless, such as lice. Among the higher insects, Pterygota, which are winged or secondarily wingless, the two common types of development are by *incomplete* and *complete metamorphosis*. Insects with an incomplete metamorphosis may differ more or less from their parents when hatched, but gradually assume the parental form with successive molts. The young or *nymphs* of such insects invariably lack wings and often have other characteristics different from their parents.

Insects with a complete metamorphosis are totally different from the parents when newly hatched and do *not* gradually assume the parental form. The early stages of such insects, usually worm-like, are called *larvae* in distinction from the nymphs of insects with an incomplete metamorphosis. Upon completion of their growth and development they go into a resting and more or less inactive stage and are then known as *pupae*. The pupa may have no special protection, as in mosquitoes and midges; it may retain the last larval skin as a protecting case called the *puparium*, as in muscid flies; or it may be encased in a *cocoon* of silk thread spun by the larva as a protection from the hostile world before going into its mummy-like pupal state, as in fleas and many moths.

Although apparently inactive, the pupal stage is one of feverish activity from a physiological standpoint, for the entire body has to be practically made over. This transformation necessitates the degeneration of almost every organized structure in the body and a reformation of new organs out of a few undifferentiated cells left in the wreckage.

The time required for this wonderful reorganization is amazingly short. Many maggots transform into adult flies in less than a week, and some mosquito larvae transform into perfect mosquitoes in less than 24 hours.

The length of life of insects in the larval and adult stages varies greatly. The larval stage may occupy a small portion of the life, as in the case of many mosquitoes and flies, or it may constitute the greater part of it. Some mayflies, for instance, live the greater part of two years as larvae, but they exist as adults not more than a few hours. As a rule male insects are shorter-lived than females. The length of life of the female is determined by the laying of the eggs—when all the eggs have been laid the female insect has performed her duty in life and is eliminated by nature as a useless being. The result is the paradoxical fact that ideal environmental conditions *shorten* the life of these insects, since they facilitate the early deposition of the eggs.

Classification of Insects

The classification of insects is based mainly on three characteristics: the type of development, the modification of the mouth parts, and the number, texture, and venation of the wings. All bloodsucking insects have mouth parts adapted in some way for piercing and sucking, but the types vary greatly in different groups. Many of the more thoroughly parasitic insects, e.g., lice, bedbugs, and "sheep ticks," have secondarily lost their wings entirely or have them in a rudimentary condition. In the whole order of Diptera the second pair of wings is reduced to inconspicuous club-shaped appendages known as *halteres*.

Not all entomologists agree on the division of insects into subclasses and orders. According to Ross (1948) there are 28 orders, 26 of which fall into the subclass Euentoma. The other two contain primitive forms, each falling into a separate subclass; they will not concern us here. The Euentoma contains all the winged insects as well as two orders of primitive wingless ones. Many entomologists, however, group all the *primitively* wingless insects—proturans, springtails, and "silver fish"—in one subclass, Apterygota, and all the others in a second subclass, Pterygota.

Many of the orders of insects comprise small or little-known groups. There are six "big" orders, members of which are known to everybody. These are (1) Orthoptera, the grasshoppers, crickets, etc.; (2) Hemiptera, the true bugs, aphids, etc.; (3) Coleoptera, the beetles; (4) Lepidoptera, the moths and butterflies; (5) Diptera, the flies, mosquitoes, etc.; (6) Hymenoptera, the bees, wasps, and ants. Important parasites and disease vectors of man and animals are found in two of these big orders, the Hemiptera and the Diptera, but others are

found in three small orders, the Anoplura or sucking lice, the Mallophaga or chewing lice (bird lice), and the Siphonaptera or fleas. The characteristics of these five orders containing parasites are briefly as follows:

Hemiptera: metamorphosis incomplete; mouth parts fitted for piercing and sucking, the piercing organs being ensheathed in the jointed labium and folded under the head; first pair of wings, unless reduced, leathery at base and membranous at tip; second pair of wings, when present, membranous with relatively few veins. Parasites: bedbugs, conenoses, kissing bugs.

Anoplura: metamorphosis incomplete; wings secondarily lost; body flattened, the thoracic segments more or less fused; legs short, the tarsi with only one or two segments, adapted for clinging to hairs of the host; mouth parts highly modified, adapted for piercing and sucking. All parasitic on mammals: sucking lice.

Mallophaga: similar to Anoplura except mouth parts fitted for chewing, being reduced to a pair of mandibles, and thorax as narrow as or narrower than the head, with not all the segments fused as much as in Anoplura. Parasitic on birds and mammals: biting or "bird" lice.

Siphonaptera: metamorphosis complete; mouth parts fitted for piercing and sucking, the piercing organs being ensheathed in the labial palpi and the maxillae modified as holding organs; wings secondarily lost. Parasites: fleas, chiggers.

Diptera: metamorphosis complete; mouth parts fitted for piercing and sucking, for sucking alone, or rudimentary; first pair of wings (absent in a few species) membranous with few veins; second pair of wings represented only by a pair of club-shaped organs, the halteres. Bloodsuckers: sandflies, mosquitoes, blackflies, tabanids, hornflies, stableflies, tsetse flies; parasites: Pupipara, maggots.

Arthropods as Parasites and Bloodsuckers

Degrees of Parasitism. All gradations exist between arthropods that are strictly parasitic throughout their lives, e.g., itch mites, hair follicle mites, and lice, and species that are purely predatory, existing entirely apart from their living restaurants except when actually feeding (e.g., mosquitoes, tabanids). Close to the strict parasite end of the series are the ixodid ticks and some adult fleas, which only intermittently leave their hosts. Somewhat farther removed are the bedbugs, triatomids, argasid ticks, and other adult fleas, which not only attend to their reproductive functions off the host but also leave to take their after-dinner naps; these forms, however, are normally inhabitants of the nests or habitations of their hosts and may be looked upon as parasites of the homes. Fleas are parasitic only as adults; certain mites and flies, only as larvae.

Effects of Bites. The effects produced by arthropod bites are brought about mainly by direct or indirect reactions to the salivary secretions. Many insects in biting create a subcutaneous pool of blood from which they suck instead of directly from a capillary. This results in most parasites that are transmitted being locally deposited in the

tissues, and not directly in the circulation (Gordon and Crewe, 1948). People commonly show immediate and delayed reactions to bites; the former reaction is due to prior sensitization and eventually may disappear as immunity develops, but the delayed reaction is due to slow-acting toxic substances in the injected saliva and usually disappears after repeated exposures before the immediate reaction does. The usual effects are local redness and swelling, with varying degrees of itching and sometimes pain, resulting in restlessness and loss of sleep. Often there are generalized allergic symptoms such as urticaria, fever, fatigue, and a rotten disposition. The unthriftiness commonly seen in animals heavily infested with ectoparasites is, however, often as much the cause of the heavy ectoparasite burden as the result of it (see p. 512). Some parasites produce *special* toxic effects, such as the paralysis caused by certain ticks (see p. 564) and the blue spots caused by crab lice.

Allergy and Immunity. The susceptibility of different individuals to the toxic effects of insect bites varies widely and is certainly dependent to a considerable extent upon sensitization. Herms cited reports of bites by the bug, *Triatoma protracta*, causing within a few minutes nausea, flushing, palpitation, rapid breathing, and rapid pulse, followed by profuse urticaria all over the body. This resembles the reactions of allergic individuals to stings of bees and wasps. The effects of itch mites and lice become pronounced only after a preliminary period of sensitization (see pp. 528 and 604).

Immunity also plays a large part. The writer has seen innumerable newcomers to Texas, including himself, who suffered intolerably from redbug bites during the first season or two of exposure to them, but who gradually became more and more immune to them. In New Jersey it is a common experience for people from inland to suffer far more severely from salt-marsh mosquitoes while vacationing on the coast than do the residents, whereas people from the coast react similarly to the inland species of mosquitoes. Mellanby thinks that most apparent cases of differences in individual attraction to insects are really differences in reaction, but the writer believes that differences in skin excretions, which vary considerably in different people, also play a part. Cherney, Wheeler, and Reed (1939) called attention to the fact that California fleas do not usually encroach on the comforts of the local population but are a source of great misery to newcomers for several months to several years.

Trager (1939) found that guinea pigs previously exposed to bites of larval or nymphal ticks developed so much immunity that larval ticks were incapable of feeding on them at all, and nymphs were unable to feed to repletion, owing to such rapid cellular reaction to the bites that

the parasites were cut off from their food. Persons susceptible to flea bites react positively to injection of flea extract, whereas immunes react negatively; most susceptible persons immunized by injections of the flea extract either become oblivious to fleas or are much less annoyed by them. Some retain their immunity several years, others for only a few weeks. McIvor and Cherney in 1943 showed that the immunized persons were not actually ignored by the fleas, but were unaware of their bites.

Although acquired immunity plays a large part, there appear to be some true instances of distastefulness of individuals to insects, based on some difference in skin metabolism which is not yet understood. One instance has been recorded in which a man's skin was highly toxic to ticks. Riley and Johannsen report a case of two brothers who volunteered to act as feeders for some experimental stock lice; the lice fed greedily on one but absolutely refused to feed on the other, even when hungry. The writer is relatively immune to nearly all arthropods and even to land leeches, but had to develop immunity to redbugs and was not immune to blackflies or *Culicoides*. He bathes with fair regularity and does not smoke, take drugs, or eat sulfur or garlic. This matter of natural repellant to arthropods needs further investigation.

The effect of diet on ectoparasites is a disputed question. Most observers, including the writer, have seldom seen healthy, well-fed animals swarming with fleas, lice, or mites, though this is often seen in sick, poorly nourished animals. Kartman (1949), however, obtained some evidence indicating loss of parasites in animals on inadequate diets. There is probably an interplay of several factors—need of the parasites for vitamins, ability of the host to develop immunity, and activity in picking or nipping the parasites.

Arthropods as Disease Transmitters

Important as arthropods sometimes are as parasites or bloodsuckers, it is in their capacity as carriers of germs or as intermediate hosts of other parasites that they have to be reckoned with as among the foremost of human foes. Since the beginning of the twentieth century many of the most important human and animal diseases have been shown not only to be transmitted by arthropods but also to be *exclusively* transmitted by particular genera or species. In addition, there are a number of other diseases, such as yaws, pinkeye, Q fever, tularemia, and anthrax, in which arthropods play an important but not exclusive role, and still others, such as many bacterial, protozoan, and helminthic infections of the digestive tract, in which they play a minor but not a negligible part.

Mechanical Transmission. The simplest method of disease transmission by arthropods is *indirect mechanical transmission*, in which the arthropods function as passive carriers of disease agents, picking them up on the bodies or in the excretions of man or animals and depositing them on food. The importance of any particular species of arthropod depends on the degree to which its structure and habits facilitate such transportation. Prominent among these indirect mechanical transmitters are houseflies and roaches.

Slightly more specialized is *direct mechanical transmission*, in which the insects pick up the germs from the body of a diseased individual and directly inoculate them into the skin sores, wounds, or blood of other animals. Biting flies, such as tsetse flies, *Stomoxys*, and tabanids, transmit blood diseases in this manner, e.g., anthrax, fowl pox, and some animal trypanosomiasis. Flies that feed on sores or wounds, such as eye flies and many muscids, transmit skin or eye diseases, e.g., yaws, trachoma, and Oriental sore. In most of these cases the organisms do not live for more than a few minutes to a few days in the vectors.

Biological Transmission. When an arthropod plays some further part in the life of the parasite or germ than merely allowing it to hitchhike, and multiplication or cyclical changes or both take place within its body, the process is called *biological transmission*. Huff (1931) proposed a classification of different types of biological transmission as follows:

1. *Propagative*: the organisms undergo no cyclical changes but they multiply as in culture tubes. Example: plague.
2. *Cyclopropagative*: the organisms undergo cyclical changes and multiply in the process. Example: malaria.
3. *Cyclodevelopmental*: the organisms undergo developmental changes but do not multiply. Example: filariae.

To these we add:

4. *Transporting* (including vertebrates as well as arthropods): the organisms invade and often become encysted in some host, specific or non-specific, after developing elsewhere, and are transported by this host to the final host. Example: *Syngamus*.

Transovarial Transmission. Transmission of disease agents to offspring by invasion of the ovary and infection of the eggs, often loosely called "hereditary" transmission, is characteristic of arthropod infections where a state of almost perfect adaptation of parasite and host has been reached. It is especially frequent in mites and ticks, which transovarially transmit some Protozoa, tularemia bacilli, rickettsias, relapsing fever spirochetes, and some viruses. In Texas fever (see

p. 576) and scrub typhus (see p. 536), transovarial transmission is a necessary part of the mechanism of transmission. Not many insect-borne infections are thus passed on from generation to generation, though some viruses may be.

Airplane Dissemination of Arthropods. Many domestic arthropods, or parasites on man, rats, or domestic animals, succeeded in making this "One World" for themselves in bygone days of slow boat travel. The airplane has made this a possibility for many more. Even if stowaway arthropods do not become established in their new surroundings, they may live long enough to pass diseases they may carry to local vectors or reservoirs.

Two unpleasant possibilities exist: (1) the introduction of more efficient vectors for diseases already in existence, e.g., *A. gambiae* to Brazil; (2) the introduction of new diseases with vectors or reservoir hosts. Ticks shipped from South Africa have arrived in this country harboring three different diseases not now known in America, and mosquitoes and ticks from Russia successfully carried with them an encephalitis virus. One shudders to think of the consequences if a yellow fever-infected mosquito were landed in India or China.

The only protection is very strict regulation of fumigation of airplanes from foreign countries. If the world is to be made safe from arthropod as well as human invaders in the future, these precautions will have to be used with the utmost care, for international air traffic is constantly expanding.

Insecticides and Repellents

Insecticides. Insects are killed by many chemicals that are injurious to vertebrates as well, such as hydrocyanic acid, sulfur dioxide, methyl bromide, arsenic, sodium fluoride, and nicotine sulfate, but fortunately are also highly susceptible to some chemicals that are much less poisonous to man and other warm-blooded vertebrates. To this group belong pyrethrum, a powder prepared from the flower heads of certain species of *Chrysanthemum*, or oil-soluble esters (pyrethrins) extracted from it; the powdered roots of *Derris* or *Lonchocarpus* (cubé), or a resin, rotenone, extracted from these; and a number of chlorinated hydrocarbons, such as DDT, benzene hydrochloride (BHC), and Chlordane. The hydrocarbons, which have revolutionized insect control by chemicals and have been largely responsible for the conquest of malaria, were developed during and after World War II. Certain organic phosphates, e.g., parathion, which are much more toxic to many agricultural pests, and also more toxic for man, were likewise developed in this period.

All of these chemicals except rotenone act primarily on the nervous system of insects and paralyze them, some almost immediately, e.g., pyrethrins, others slowly, e.g., DDT and BHC. Most of the insecticides named above can be absorbed either through the cuticle or the stomach, but the pyrethrins only through the cuticle.

When insecticides come in contact with insects as solid particles in dusts, they usually get into the alimentary canal when the insects fastidiously groom themselves. In addition, the inert dust particles may abrade or adsorb the lipoid epicuticle, thus facilitating outward passage of water and inward penetration of the chemicals through the cuticle. Although the chlorinated hydrocarbons readily penetrate the cuticle when in a dry crystalline state, since they are soluble in the lipoids of the epicuticle, they do this even more readily when dissolved in oil. DDT is peculiar in having a special strong affinity for chitin, by which it is rapidly adsorbed.

Pyrethrins are not volatile but they are unstable, therefore have little residual effect. This difficulty can be overcome to some extent by the addition of piperonyl butoxide, which for some unknown reason not only increases the toxicity of pyrethrins but also makes them effective for several months. Pyrethrum powders gradually deteriorate. They are used in kerosene solution or in aqueous suspensions of extracts in acetone or alcohol. They are toxic to all invertebrates except Protozoa, and to fish; they are detoxicated in the alimentary canal and tissues of higher animals.

Derris or cubé powders or rotenone, the principal active substance in them, were first known as fish poisons, but they are also very toxic to insects. Their principal uses for parasitic insects are against cattle warbles, *Hypoderma* (see p. 765), the "sheep-tick," *Melophagus* (p. 688), and ticks.

Of the chlorinated hydrocarbons DDT has been most extensively used, and is highly effective against most parasitic and disease-carrying insects, except mites and ticks, cattle grubs, and fly maggots. However, some insects, and particularly houseflies, quickly develop resistance to this as well as to other chlorinated hydrocarbons, and may become completely immune to it. Several mechanisms are involved, mainly change to non-toxic DDE and other derivatives by enzymes, and storage of DDT in fat, where it is relatively harmless. Piperazine cyclonone strongly inhibits the change to DDE and therefore acts as a "synergist," enhancing the action of DDT. Thus far, mosquitoes have not shown as much aptitude as houseflies for tolerating DDT, although moderate degrees of resistance have been observed in some mosquitoes (see p. 736). Unfortunately when an insect has developed resistance

to one chlorinated hydrocarbon it more quickly develops it to others. In 1948 headlines even in scientific journals proclaimed that a flyless age was in sight; today, having had to return to the troublesome path of environmental sanitation from the exploded royal road of chemical extermination, we see that the flyless age has again disappeared over the horizon.

Benzene hexachloride (BHC) contains a number of isomers, of which only the γ isomer, also known as Gammexane or Lindane, is highly effective against arthropods. Commercial BHC should contain 10 to 13 per cent Lindane, whereas purified Lindane approaches the ivory soap standard of purity. Lindane lacks the pungent odor of BHC which makes the latter undesirable in houses. Lindane is more effective than DDT against mites, roaches, eggs of lice, triatomids, and fly larvae. Unlike DDT, Lindane is volatile, so has fumigant value but less residual effect.

Chlordane, because of its fumigant action, is highly effective against heavily sclerotized insects like roaches, fleas, beetles, and ants; but it is more toxic to man and animals when inhaled, ingested, or in contact with the skin than is either DDT or Lindane; it is therefore not recommended for general use in homes.

Other chlorinated hydrocarbons which may be used for flies, mosquitoes, etc., under some circumstances are Aldrin, Dieldrin, and Toxaphene, but they are more toxic to man than those mentioned above. There are also a number of analogues of DDT. Of these DDD is as effective as DDT against mosquito larvae and is less toxic to fish. Methoxychlor is the least toxic for man by mouth, and therefore the safest residue on fruits, vegetables, or milk. Since it is not stored in animal fat, it is an excellent spray for dairy cattle, and for many insects it is as effective as DDT.

Methods of Application. Insecticides are dispersed as dusts; as solutions, emulsions, or water suspensions designed to leave surface deposits with which the insects will come in contact (residual sprays); or as finely divided particles in mists, aerosols, or smokes which come in direct contact with the insects (space sprays); as fumigants; or as additions to the food of the hosts. Stomach poisons are extensively used for agricultural insects, applied as sprays to leaves or fruit or mixed with food, but are little used against ectoparasites or disease vectors. Paris green powder for *Anopheles* larvae was an exception. A few attempts have been made to obtain insecticidal or at least repellent effects by feeding chemicals to hosts; the results have not been too good, but they suggest that further research might be worth while (see pp. 613 and 765).

DUSTING. Dusts most commonly used for insects of importance to the health of man or animals are 5 per cent to 10 per cent DDT, BHC, chlordane, or other chlorinated hydrocarbons, diluted with pyrophyllite or talc; these are useful for argasid ticks, roaches, triatomids, bedbugs, fleas, head lice, and preflood treatment of rice fields for mosquito larvae.

RESIDUAL SPRAYS. For residual sprays, the chlorinated hydrocarbons can be applied as solutions in oil (usually kerosene); emulsions made by mixing concentrated xylene solutions with water and an emulsifier; or suspensions made either by mixing with water-wettable powders (usually half insecticide and half pyrophyllite), or powders containing detergents. Oil films, as long as they last, are more effective than dry crystalline residues; addition of a small amount of non-volatile oil like lanolin to the kerosene diluent coats the crystals with an oily film which prolongs their heightened effectiveness, and should also make them weather more slowly outdoors.

For residual spraying DDT, etc., are applied in 5 per cent emulsions, solutions or suspensions to give a residue of 200 mg. per square foot; emulsions are best indoors, since they do not produce as obvious films. Outdoors a small amount of rosin or non-volatile oil may be added. Surfaces treated thus remain toxic to insects resting on them for 3 to 6 months or even longer. On absorbent surfaces such as mud bricks, of which houses in the tropics are so commonly built, water suspensions of wettable powders adhere to the surface better. If DDT soaks in, its effectiveness is lost; but BHC and chlordane, being volatile, have a prolonged fumigant effect, which, however, is not always sufficient to be lethal. Particle size is important, and a compromise has to be found between the greater effectiveness of small particles of 10 to 20 μ and the greater persistence and less absorption of larger particles on absorbent surfaces. The effectiveness of DDT on mud bricks is also influenced by the chemical nature of the mud; those containing much iron oxide detoxicate DDT quickly. Prior application of whitewash to mud surfaces increases the effectiveness of DDT.

SPACE SPRAYS. For space sprays indoors, combinations of DDT and pyrethrum dissolved in kerosene and sprayed from hand sprayers are fairly effective in small rooms. Aerosols, however, are much better. They are prepared by dissolving 15 per cent of an oil concentrate of DDT and pyrethrum, plus sesame oil as a synergist, in 85 per cent Freon. The pyrethrum gives a quick knockdown, and the DDT then finishes the job of killing. The Freon is liquid while under pressure in the "bomb," but immediately evaporates when released, liberating the insecticide in minute particles 2 to 10 μ in diameter, as compared with

droplets 5 to 150 μ in diameter from atomizers. The fine particles float in the air and permeate every crevice. Outdoor space sprays consist of fogs, mists, or smokes produced by special generators on trucks or airplanes, using oil solutions of the insecticides. Little residual effect can be expected from such applications.

WATER TREATMENTS. For application to standing water to kill aquatic larvae of mosquitoes or *Culicoides*, either dusts or oil emulsions, or aerosols (from airplanes) are commonly used. A dose rate of 0.05 to 0.1 lb. of DDT per acre is sufficient except where there is dense vegetation. Even where there is dense vegetation 0.1 to 0.2 lb. per acre kills 98 to 99 per cent of mosquito larvae, as well as reducing the adults to a like degree. In early experiments on some ponds it was a mystery why even untreated control ponds became free of mosquito larvae, until it was observed that ducks flying from pond to pond carried enough DDT on their feathers to extend the experiment! The chief disadvantage is the toxicity of DDT to fish. Where fish are more important than dead mosquitoes, 0.05 p.p.m. of water should not be exceeded, or else a Paris green dust substituted. The latter, however, is effective only against *Anopheles* larvae, and does not kill eggs or pupae. Special methods of application against blackfly larvae in running water are discussed on p. 665.

SKIN APPLICATIONS. For application to animals, dips, sprays, or dusts containing chlorinated hydrocarbons are more effective and safer than the arsenic or sodium fluoride dips formerly used. Since DDT in powder form is not absorbed through the skin, it can be used on human skin or clothing to kill lice, fleas, or mites.

FUMIGATION. For fumigation to destroy indoor pests such as mites, argasid ticks, bedbugs, fleas, and rats in houses, barns, ships, etc., hydrocyanic acid gas (HCN) has been extensively used, but it is very toxic to all forms of life. HCN fumigation should be done only by trained and experienced exterminators. With the advent of aerosols its use is largely outmoded except against rats. Sulfur dioxide is another fumigant formerly widely used, generated by burning sulfur in a humid atmosphere. It has the disadvantage of tarnishing metals and bleaching fabrics. Methyl bromide is a very satisfactory fumigant for use in spaces that can be tightly sealed, or enclosed under airtight plastic coverings, e.g., for stored products in cars or bins, vermin in railway cars, etc. It can also be used for killing rodents and their ectoparasites in burrows in the ground. Devices for application which are practically foolproof are available. Special fumigants are the fumes from naphthalene flakes scattered on the floor to kill fleas; the fumes

of nicotine sulfate painted on roosts to kill chicken lice; and *p*-dichlorobenzene to kill flies in deep latrines and garbage pits.

Repellents. These are substances that can be applied to the skin or clothing to keep insects, mites, or ticks from biting—they should be non-toxic, non-sensitizing, have no objectionable odor, and have lasting effect. Prior to World War II oil of citronella or other essential oils were most widely used, but the effect was too temporary. More recently, out of thousands of repellents tested, several good ones have been found; but no single one is equally effective against all kinds of arthropods, or even against different species of mosquitoes.

Widely used now are Indalone, particularly good against biting flies and some mosquitoes; Rutgers 612, best for most mosquitoes; dimethyl and dibutyl phthalate, good against fleas and mites as well as many mosquitoes; and benzyl benzoate, hexylmandalate, benzil, dephenyl carbonate, and *n*-butyl acetanilide, all particularly effective against mites and ticks. The standard U. S. Army repellent in use now (M-1960) consists of equal parts of *n*-butyl acetanilide, propanediol, and benzyl benzoate, with 10 per cent Tween 80 emulsifier. Clothing impregnated with 2 grams per square foot of M-1960, or the tick repellents mentioned above, applied in acetone solutions, remains highly protective against mites and ticks even after six or seven washings. Applied as dusts to the skin and in 4-in. barriers around openings in clothes, they are effective for many hours. An ounce of dibutyl phthalate rubbed into the clothing as a powder keeps off redbugs even after many washings, and is effective against schistosome cercariae as well (see p. 292). Benzyl benzoate both repels and kills mites.

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The Acarina (Mites) and Pentastomida

ACARINA (EXCEPT TICKS)

Acarina in General. The order Acarina of the class Arachnida includes a large number of species commonly known as mites or ticks. Most of them are very small, some barely visible to the naked eye, but some of the ticks reach half an inch or more in length. The ticks, although constituting only one of the five suborders of Acarina, are distinct and important enough to warrant special consideration in a separate chapter (24).

There is a great variety of body form in the Acarina, some appearing quite grotesque. The majority are more or less round or oval, without division into head, thorax, or abdomen, but some have a suture dividing the body into anterior and posterior divisions (Fig. 161). There is no true head, but the mouth parts are borne on an anterior part that is usually rather distinctly set apart, called a gnathosoma or capitulum. There are two pairs of mouth parts, the chelicerae and the pedipalps or palpi (Figs. 160, 166). The chelicerae usually end in little pincers made up of a movable and an immovable digit, but they may be modified into needle-like structures, as in *Dermanyssus*, or in other ways. The palps usually consist of four to six segments, sometimes modified as a thumb-and-claw. In the ticks the ventral wall of the gnathosoma is elongated between the palpi and armed with recurved teeth (Fig. 166). In the first or larval stage there are only three pairs of legs, but after the first molt when the mite or tick becomes a nymph, a fourth pair of legs is acquired. The legs typically consist of six or seven segments called the coxa, trochanter, femur (sometimes divided), genis, tibia, and tarsus. The tarsi usually bear claws and often a sucker-like caruncle, sometimes on long stalks (Fig. 154).

Many Acarina have pouches on the midgut which give them great food capacity; a well-fed female tick gets so distended that she looks more like a bean than an arthropod. For breathing, many mites have tracheae which open by one to four pairs of stigmata or spiracles. In

the Mesostigmata and ticks the adults have only one pair, situated near the third coxae (Fig. 166), and in the Mesostigmata there is a chitinous tube or *peritreme* leading forward from each spiracle. In the Proto-stigmata the spiracles are on or near the gnathosoma, whereas in the Sarcoptiformes there are either no spiracles (or tracheae) or many inconspicuous ones.

The genital apertures open at various places on the ventral surface of the abdomen, and are closed by specialized plates. Usually there are morphological differences between the sexes, but sometimes the sexes are not easily distinguished.

Many mites are free-living and prey upon decaying matter, vegetation, stored foods, and the like; some are predaceous and feed upon smaller animals; some are aquatic, even marine; and many are parasitic on other animals during all or part of their life cycle. Some of the parasitic forms are among the most important disease vectors, and the members of at least one group of free-living mites (Oribatei) serve as intermediate hosts for tapeworms (Anoplocephalidae).

Life History. There are usually four stages in the development of mites and ticks: the egg, the larva, the nymph, and the adult (see Figs. 174, 175). The eggs are usually laid under the surface of the soil or in crevices or, in some parasites, under the skin of the host. After a varying period of incubation the larva hatches in the form of a six-legged creature, often quite unlike the parent. After a single good feed the larva rests, sheds its skin, and appears with an additional pair of legs and a body form more closely resembling that of the parent but without developed sexual organs. The nymph thus produced feeds and molts once or several times and finally, after another period of rest during which the body is once more remodeled, molts again and comes forth as an adult male or female. There are many modifications in the development due to the slurring over of certain phases or interpolation of others, e.g., the molting of some larval ticks and mites in the egg or just after hatching but before feeding, and the occurrence of additional intermediate stages in hydrachnids, trombiculids (p. 533), and tyroglyphids (p. 541).

Some mites have become adapted to live as internal parasites in the lungs and air sacs of snakes, birds, and mammals, and there are records of mites which are not normally parasitic at all living and multiplying in the human urinary bladder; but all the species normally infesting man are either external or subcutaneous in their operations.

Classification. Baker and Wharton (1952) in a modification from the classification of Vitzthum (1940-1942), classify the Acarina as follows:

- Suborder **Onchopalpida**. Palpi with claws as on the legs; 2 or more pairs of stigmata on body. Contains no parasitic forms although a species of *Holothyrus* in Mauritius is said to secrete a poison that may cause death of ducks and illness of children.
- Suborder **Mesostigmata**. Body well-chitinized, with dorsal and ventral plates; gnathosome small, anterior; 1 pair of lateral stigmata near third coxae, each with a sinuous, chitinous peritreme leading forward; tarsi usually with claws and caruncles. Contains several families of interest:
- Halarachnidae**, including parasites of respiratory passages of seals (*Halarachne*), and monkeys (*Pneumonyssus*).
- Entonyssidae**, lung parasites of snakes (*Entonyssus*).
- Rhinyssidae**, nasal parasites of birds.
- Dermanyssidae**, bloodsucking "red mites" of birds and mammals (*Dermanyssus*, *Bdellonyssus*, *Allodermanyssus*).
- Laelaptidae**, bloodsucking mites of rodents, etc.
- Suborder **Ixodides**. Ticks; size large; body leathery with or without plates; 1 pair of lateral spiracles near fourth coxae but no tubular peritreme; hypostome present, armed with recurved teeth. Includes 2 families:
- Argasidae**, "soft" ticks; no dorsal shield; body tuberculated; gnathosome ventral.
- Ixodidae**, "hard" ticks; dorsal shield present; body not tuberculated; gnathosome anterior.
- Suborder **Trombidiformes**. One pair of stigmata on or near gnathosome; palpi free, highly developed; chelicerae developed for piercing. Contains several families of interest:
- Demodicidae**, hair follicle mites; worm-like, with very short legs.
- Pyemotidae** (= **Pediculoididae**), louse mites; a club-shaped organ between coxae 1 and 2; legs all similar; larvae hatch and develop to maturity in sac-like abdomen of female.
- Tarsonematidae**, plant pests; occasionally found in human lungs or intestine.
- Trombiculidae**, harvest mites with parasitic larvae (redbugs or chiggers); tarsus of palpus forms thumb closing against tibia; body covered with feathered hairs; larvae with dorsal shield with hairs and a pair of pseudostigmatic organs; body of adult divided into two sections.
- This order also includes water mites, many parasites of arthropods, and mites that prowl in foods, fur, or feathers hunting other mites (*Cheyletidae*).
- Suborder **Sarcoptiformes**. No well-developed stigmata or conspicuous tracheae. Chelicerae usually scissors-like, for chewing; palpi simple; oral suckers often present.
- Group **Acaridiae**. Soft-skinned; without stigmata or prominent club-shaped pseudostigmatic organs; tarsi with caruncles. Includes following families of interest:
- Acaridae** (= **Tyroglyphidae**), **Glycyphagidae** and related families, usually called tyroglyphids, infesting foods and causing grocer's itch.
- Sarcoptidae**, itch mites; soft, unsegmented body; skin with fine striations interrupted by scaly areas; legs short; includes *Sarcoptes*, *Notoedres*, and *Cnemidocoptes*.
- Psoroptidae**, mange mites; dorsal shield present; bell-shaped caruncles on stalks; abdomen of male bilobed posteriorly; includes *Psoroptes*, *Chorioptes*, and *Otodectes*. Although placed by Baker and Wharton in the

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Trombiculiformes, *Psorergates ovis*, causing a mange-like disease of sheep, probably belongs here.

Group **Oribatei**. Heavily chitinized; prominent club-like pseudostigmatic organs; no caruncles. Free-living "beetle mites." Includes numerous families, of which at least seven contain species that serve as intermediate hosts of anoplocephalid tapeworms.

In the present chapter we shall consider all the Acarina except the ticks, which will be dealt with separately in Chapter 24.

Itch and Mange Mites (Sarcoptidae and Psoroptidae)

Species. The minute rounded or oval, short-legged, flattened mites of the family Sarcoptidae are the cause of scabies or "itch" in man; similar mites belonging to the related family Psoroptidae (see p. 524) are the cause of mange or scab in many kinds of animals. The species that attacks man, *Sarcoptes scabiei*, is so similar to forms of *Sarcoptes* causing mange in many other animals—dogs, foxes, cats, rabbits, ruminants, horses, and pigs—that all of these are considered mere biological varieties of one species. These varieties are so adapted to the hosts in which they have been living that it is difficult to transfer them to other hosts. Other genera of these two families attack various domestic animals.

Following is a key to the most important genera:

- | | |
|---|------------------------|
| 1a. Posterior pairs of legs nearly or quite concealed under abdomen | 2. |
| 1b. At least third pair of legs projecting | 3. |
| 2a. Dorsum with spines and pointed scales (Fig. 154) | <i>Sarcoptes</i> . |
| 2b. Dorsum with spines and rounded scales | <i>Notoëdres</i> . |
| 2c. No dorsal spines or scales (Fig. 155) | <i>Cnemidocoptes</i> . |
| 3a. Pedicles of tarsal suckers very long | <i>Psoroptes</i> . |
| 3b. Pedicles short | 4. |
| 4a. ♀ with suckers on legs 1, 2, 4; with posterior abdominal lobes | <i>Chorioptes</i> . |
| 4b. ♀ with suckers on legs 1, 2; abdomen without lobes | <i>Otodectes</i> . |

Notoëdres cati causes a very severe and sometimes fatal mange in cats; it temporarily infests man but soon dies out. *Psoroptes* does not burrow under the skin but causes "scab" in ruminants and horses; *Chorioptes* causes foot scab in horses, and *Otodectes* ear mange in carnivores; *Cnemidocoptes* has two species attacking chickens, one causing scaly leg, the other "depluming" mange. *Psorergates ovis*, less than half the size of *Sarcoptes*, causes mange of sheep and injury to the wool.

***Sarcoptes scabiei*.** The itch mites, *Sarcoptes scabiei* (Fig. 154), are minute whitish creatures, scarcely visible to the naked eye. They are nearly round, and the cuticle is delicately sculptured with numerous wavy parallel lines, pierced here and there by stiff projecting bristles or

hairs. They have no eyes or tracheae. The mouth parts, consisting of a pair of minute chelicerae and a pair of three-jointed triangular pedipalps, are attached to a capitulum or gnathosome in the front of the body. The legs are short and stumpy and are provided with sucker-like

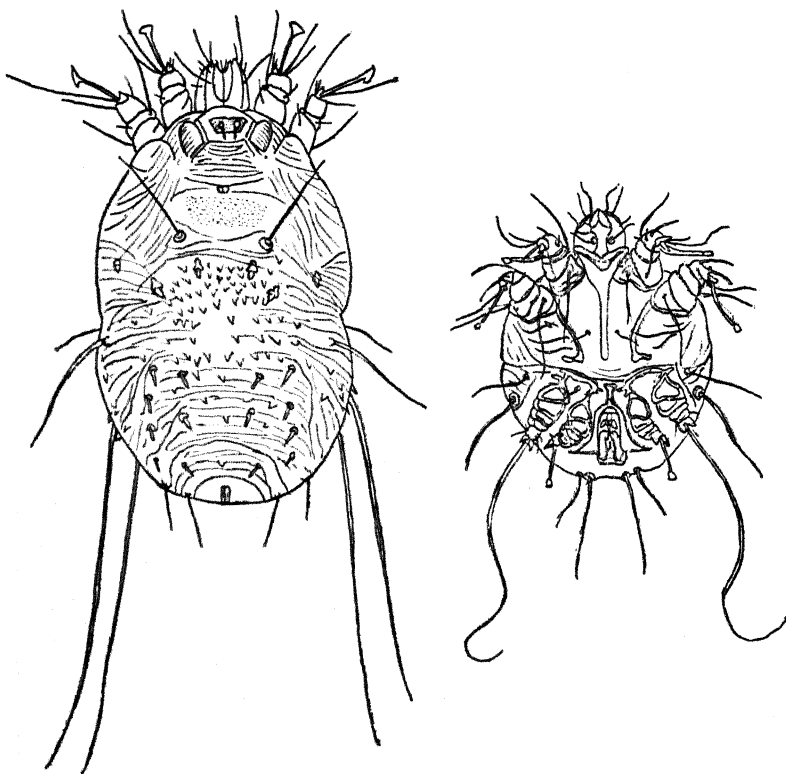


FIG. 154. *Sarcoptes scabiei*, itch mite. Left, ♀; right, ♂; $\times 150$. (♀ adapted from Buxton, *Parasitology*, 13, 1921. ♂ after Bedford from Mönnig, *Veterinary Helminthology and Entomology*, 1949.)

organs at the tips of long unjointed pedicels in the first two pairs of legs in the females, and in the first, second, and fourth pairs in the males; the other legs terminate in long bristles. The number of legs with pediceled suckers, and whether or not the pedicels are jointed, are important characters in differentiating other genera. In the human itch mite the male is less than 0.25 mm. in length and the female about 0.3 to 0.4 mm. in length.

The impregnated females excavate thin tortuous tunnels in the epidermis (Fig. 156), especially where the skin is delicate and thin. The

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tunnels measure a few millimeters to over an inch in length and are usually gray from the eggs and excrement deposited by the female as she burrows; under a lens they look like a chain of minute grayish specks punctuated at intervals by a tiny, hard, yellow blister. The daily excavations of a mite amount to 2 or 3 mm.

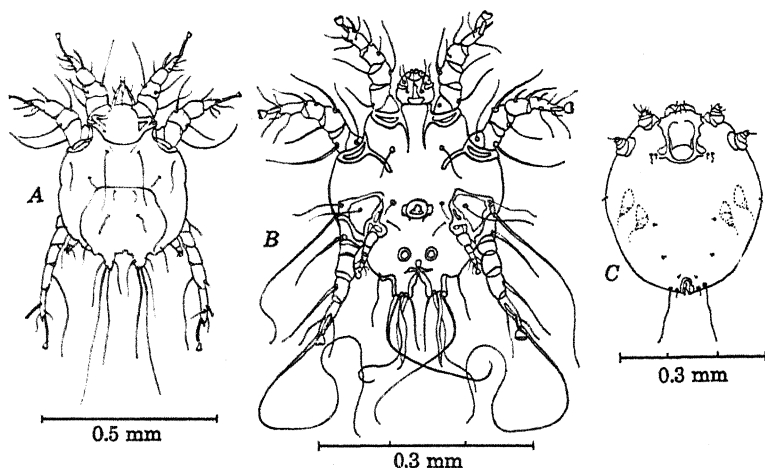


FIG. 155. A, *Psoroptes* ♂, dorsal view; B, *Chorioptes* ♂, ventral view; C, *Cnemidocoptes* ♀, dorsal view. (After Whitlock, *Practical Identification of Endoparasites for Veterinarians*, Burgess.)

Life Cycle. The eggs, about 160 μ long, are laid in the burrows at the rate of 2 or occasionally 3 a day until a total of about 35 to 50 have been laid, after which the female dies, usually at the end of a single tortuous burrow. The eggs hatch in a few days into larvae which resemble the adults except in minor details and in the absence of the fourth pair of legs. The larvae transform in 2 or 3 days into nymphs. The nymphs commonly build burrows for themselves and molt twice, the second time becoming adult male and female mites. The duration of the two nymphal periods is 3½ to 6 days, the entire development of the mites therefore requiring 8 to 14 days. The adults live about 4 weeks.

The mites are not necessarily nocturnal as was formerly supposed, but wander about on the surface of the skin when it is warm, most frequently when the host is in bed. The males are usually stated to be short-lived and to remain on the surface of the skin, but Munro in 1919 questioned this. The males are not, however, very commonly found. The young impregnated females make fresh excavations of

their own. Since there is a new generation about every 3 weeks, the rate of increase is potentially enormous, yet according to Mellanby (1943) the average number of adult females in an infested person is less than twelve, and not one person in ten has over thirty.

THE DISEASE. The "itch" (scabies) is a disease which has been known much longer than it has been understood; it was formerly attributed to "bad blood." In the past, itch swept over armies and populations in great epidemics, but it has decreased with civilization and cleanliness.

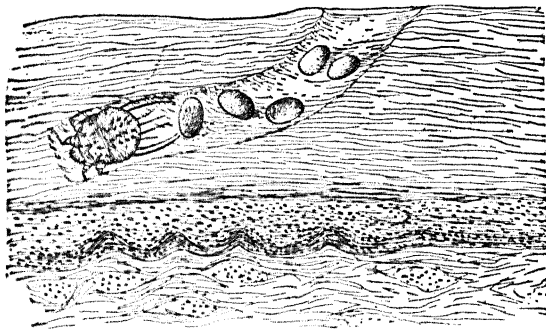


FIG. 156. Diagrammatic tunnel of itch mite in human skin, showing ♀ depositing eggs. About $\times 30$. (Adapted from Riley and Johannsen, *Medical Entomology*, 1938.)

As shown by Mellanby (1943, 1944), the intense itching that characterizes the disease does not begin until a month or so after an initial infection, when the skin has become sensitized; prior to this there is very little discomfort. After 6 weeks there is enough irritation to disturb sleep, and after about 100 days the irritation may be continuous and unbearable. In previously uninfected persons the mites reach a peak population of 50 to 500 in 7 to 16 weeks, after which the number declines sharply to 10 or less. The lesions, however, get worse and often appear where there are no longer any mites, and secondary infections, such as impetigo, develop. In reinfections intense local irritation, redness, and edema begin in 24 hours, often causing the parasites to be removed by the fingernails or to leave voluntarily an environment that is unfavorable for them because of edema or septic infections. The itching may persist for days or weeks after the mites are removed or killed. In reinfections the average number of mites present is only 3 or 4. A few mites may, however, persist for a very long time.

The mites invade the skin of the hands and wrists most frequently. Mellanby found them there in 85 per cent of cases, but they also attack

the groin and external genitals, breasts, feet, or other parts. The head is rarely attacked, although a severe "crusted" form of the disease called Norwegian itch occurs in Europe and attacks the head as well as other parts.

Although the burrows of the mites are often sufficiently characteristic to make a diagnosis possible, it should usually be confirmed by finding the mites, which are not in the vesicles but usually near them at the ends of the burrows. Scrapings from the blind ends of the burrows should be examined microscopically for adults or larvae; the latter are only about 0.15 mm. long.

EPIDEMIOLOGY. Infection can result only from the passage of male and female mites or of an impregnated female from an infected to a healthy individual. Normally this takes place by actual contact, rarely in the daytime on account of the secretive habits of the mites, but commonly at night, especially from one bedfellow to another. Mellanby found that transmission through bedding or clothing is relatively rare, except after contact with the small percentage of cases having a large number of mites. He was uniformly successful in establishing infections in previously uninfected volunteers by transfer of young impregnated mites but never younger stages. The adults can live apart from a host for 2 or 3 days under favorable conditions. It is possible for infection to be derived from many animals, though the mites, once adapted for several generations to a given host, do not often survive a transfer to a different species of host for more than a few days.

TREATMENT AND PREVENTION. Since the mites and their eggs are situated beneath the skin, superficial treatments with home remedies seldom eliminate all the mites, although they may reduce their numbers. For many years the standard remedy was sulfur ointment ($\frac{1}{2}$ oz. of sulfur in 16 oz. of lard or lanolin) applied after softening the skin with soap and warm water. During World War II benzyl benzoate was found to be easier to apply and 100 per cent effective. Mellanby recommended a lotion consisting of equal parts of benzyl benzoate, soft soap, and isopropyl alcohol, but this often causes considerable skin irritation. Slepian (1944) developed an effective treatment using a benzyl benzoate lotion.

Even more effective in treatment is Lindane, applied either as 1 per cent in vanishing cream at the rate of 30 to 50 grams, or sprayed on the skin in a 1 per cent emulsion. This treatment is also effective for lice. The principal disadvantage is the cost. To obtain complete cures it is necessary to treat the entire body below the head, and also to treat bed mates, for the infestation almost always spreads thus in

families. Lindane applications are also useful in various types of mange in animals.

Prevention of this annoying infection consists merely in avoiding contact with infected individuals and of shunning public towels or soiled bed linen. When introduced among groups of previously uninfected individuals, scabies may cause extensive epidemics.

Treatment of Mange in Animals. Most forms of animal mange respond to dips or applications in oil or salves of Lindane; in dips for sheep and cattle and foot baths for horses 0.06 per cent γ -BHC is adequate; for dogs and pigs spraying or application in oil, using 0.1 per cent, is recommended, but this must be used with care for cats. Dips of lime sulfur solution are also useful for sheep, cattle, and pigs. For scaly-leg of chickens 0.1 per cent Lindane is applied to the legs.

Hair Follicle Mites (*Demodex*)

The hair follicle or face mite, *Demodex folliculorum* (Fig. 157), of the family Demodicidae, is a worm-like creature, very unmite-like in general appearance, which lives in the hair follicles and sebaceous

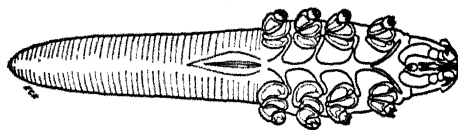


FIG. 157. *Demodex folliculorum*, hair follicle mite, $\times 200$. (After M gnin, from Faust in Brennenman, *Practice of Pediatrics*, Prior.)

glands of various mammals. In man it occurs especially on the face and has been found in the ear wax. In dogs it has also been found in lymph glands. Numerous forms from various animals have been described as different species, but they are all strikingly alike and the extent of their specificity is questionable.

The worm-like appearance of the adult mites is due to the great elongation of the abdomen, which is marked by numerous fine lines running around it. The head is short and broad, and the four pairs of legs, all similar, are short, stumpy, three-jointed appendages. The females are 0.35 to 0.40 mm. long, the males a little smaller.

The multiplication of these mites is slow. The eggs hatch into tiny six-legged larvae in which the legs are mere tubercles. It requires four molts to bring the larvae to sexual maturity.

The occurrence of these parasites in the hair follicles of man, particularly about the nose, is extremely common; in Germany Gmeiner (1908) found them in 97 of 100 random examinations of individuals

with healthy skins. The presence of the mites rarely causes any symptoms whatever, and in man they should probably be considered entirely harmless parasites. Their occasional discovery in cases of acne, blackheads, and other skin conditions leads to suspicion that they are the cause of the condition. Actually, however, Gmeiner found them much less frequently in cases of acne and blackheads than he did in healthy skins and thought that the altered contents of the diseased follicles and skin glands was unfavorable for their development. In dogs, on the other hand, *Demodex* causes a severe and sometimes fatal form of mange. Some authors think the infection is extremely common in dogs, as it is in man, but that it produces symptoms only under conditions of poor health, vitamin deficiencies, etc. There is a scaly form of the disease in which the skin becomes red, wrinkled, and scaly, and loses its hair, and a pustular or abscessed form in which the skin is invaded by staphylococci, to which dogs are usually resistant. Similar forms occur in cattle, pigs, goats, and horses.

The method of transmission of the mites to another host is not definitely known, but it is probable that the adults wander on the surface of the skin at times and may then be transmitted by direct contact or by towels, as are itch mites. Since generation after generation may be produced on a single host the infection is potentially indefinite in its duration.

In dogs transmission takes place in a very irregular manner, and frequent instances are cited of infected dogs associating for a long time with uninfected ones without spreading the disease. Experiments with transmission of the canine follicle mite to man have invariably failed. No entirely satisfactory treatment is known, but promising results have been obtained on demodectic mange of various animals by rubbing in benzene hexachloride in lanolin ointment or brushing with a solution in linseed oil. Phenothiazine applications also are said to be effective in dogs. Good food and hygienic conditions are important; not infrequently the disease disappears spontaneously. In 1946 good results were reported from treating mangy dogs with niacin, a vitamin in which dogs are frequently deficient.

Redbugs or "Chiggers" (Trombiculidae)

There is probably no creature on earth that can cause more torment for its size than a redbug, but in the Far East even this distinction is not enough. In that area some species add injury to insult by transmitting a disease, scrub typhus, which during World War II caused more trouble in the Pacific area than any other insect-borne disease except malaria. These mites are also suspected on epidemiological

grounds of transmitting epidemic hemorrhagic fever (Traub et al., 1954). This is a virus disease in Siberia, Manchuria, and Korea which causes fever, dilation and increased permeability of capillaries, kidney damage, etc., and is fatal in about 5 per cent of cases (Brown, 1954). A field mouse, *Apodemus agrarius*, is believed to be a reservoir host.

The redbugs (Fig. 158) are the six-legged larvae of mites of the family Trombiculidae, formerly considered a subfamily of Trombiculidae. The larvae of the latter are parasitic on insects, whereas

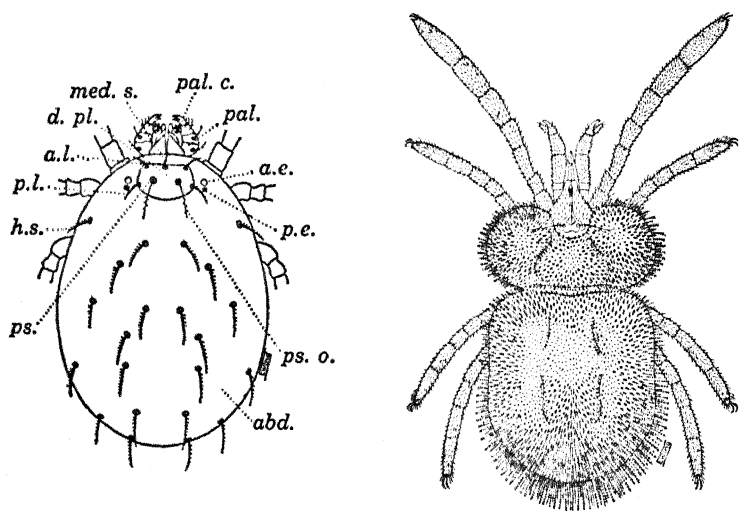


FIG. 158. Left, common American redbug or chigger, *Entrombicula alfreddugesi*, about $\times 160$. Right, adult ♀ of same. (After Ewing: left, *J. Wash. Acad. Sci.*, 28, 1938; right, *Proc. Biol. Soc. Wash.*, 38, 1925.)

the trombiculid larvae are always parasitic on vertebrates. This, as with the Hydrachnidae, is a biological trick for better dispersal. The nymphs and adults are velvety, scarlet-red mites that are free-living. It has been generally believed that they feed on organic debris, but their principal food seems to be insect eggs or minute insect larvae.

The parasitic larvae, called redbugs, rougets, chiggers, harvest mites, scrub mites, or various local names, are minute reddish or orange creatures barely visible to the naked eye (about 0.2 by 0.15 mm.) when unfed. Just behind the capitulum is a small dorsal scutum ornamented with five (in some species six) feathered hairs and a pair of pseudostigmatic organs (Fig. 159B, C) from which arise sensory hairs, long and slender in the human species, club-shaped in certain others. There are also feathered hairs on other parts of the body and on the palpi

and legs. Genera and species are distinguished by details of the dorsal scutum and of the hairs on the palpi and legs.

Life History. The life cycle has been worked out completely in only a few species but is probably similar for all; it is peculiar in that extra cuticular coverings are produced between the usual stages, and that the fleshy parts of the legs are resorbed and totally new legs are

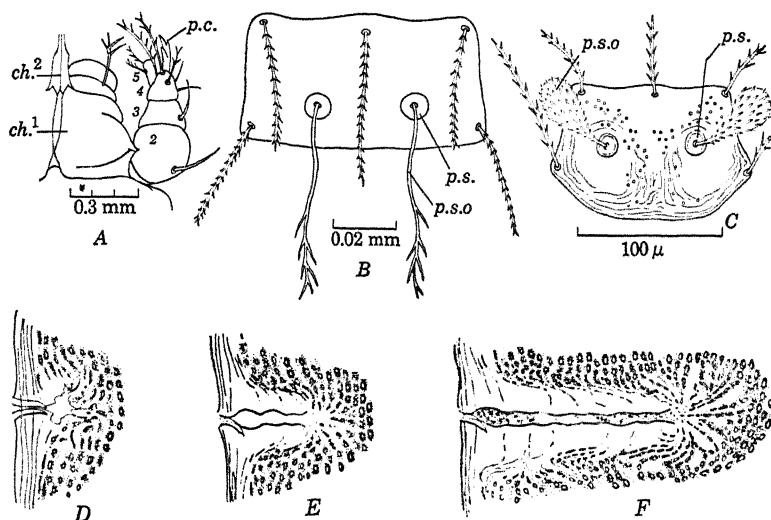


FIG. 159. A, Gnathosoma or capitulum of *Trombicula akamushi*; *ch.1*, basal segment of chelicera; *ch.2*, distal segment of chelicera; *p.c.*, palpal claw; numbers indicate second to fifth segments of palpus. B, scutum of *Trombicula akamushi*. C, same of *Neoschöngastia*; *p.s.*, pseudostigma; *p.s.o.*, pseudostigmatic organ. D-E, stages in formation of tissue canal or stylostome by a trombiculid larva alternately injecting saliva and withdrawing tissue nutrients. D, initial injection of saliva. E, tissue canal forming. F, flow of nutrient along well-formed tissue canal. (A and B adapted from Wharton, *Proc. Ent. Soc. Wash.*, 48, 1946. C, from Brennan, *J. Parasitol.*, 37, 1951. D-F, after Jones, *Parasitology*, 40, 1950.)

formed in each successive stage. The eggs, laid singly or in small groups, are deposited on the ground. After the general body form is laid down in the egg a cyst-like membrane develops around the embryo, which is exposed by the splitting of the egg shell. This stage, called a deutovum, develops in about 6 days. Six days later the fully developed larva hatches, attaches itself to a vertebrate host at the first opportunity, and remains attached for a few days to a month. Williams found that the larvae may pass the winter comfortably holed up in the ears of rabbits or squirrels. After engorgement the larva drops off and molts; meanwhile the tissues of the appendages undergo lysis, and a thin chitinized shell is laid down under the old larval skin; this

stage is called a protonymph or nymphochrysalis. In a few days an eight-legged nymph develops inside and emerges. After feeding and growing, the nymph changes to a preadult or imagochrysalis, from which an adult male or female emerges in about 6 days or more. The nymphs and adults (Fig. 158) are similar in appearance, the nymphs being about 0.5 mm. and the adults about 0.75 to 1 mm. long. They probably feed principally on insect eggs or minute larvae, and may do away with appreciable numbers of eggs of *Aedes* and *Psorophora* mosquitoes which are laid on dry ground in their hunting grounds.

Important Species and Their Habits. Redbugs are anchored to the skin surface by a tissue reaction to the irritating saliva that is superficially injected. The redbugs then drool into the skin; the saliva dissolves the skin tissue as it penetrates, forming a tubular structure in the skin called a stylostome, nearly as long as the body of the mite and filled with semidigested tissue debris on which the mite feeds (Fig. 159, D-F). The mites do not feed on blood, although their red color when engorged gives that impression.

Some redbugs show marked host preferences, different species normally confining themselves to such hosts as rodents, bats, birds, or reptiles, respectively, but a few do not show much discrimination and are content to drool into the skin of almost anything they can get access to, whether it be a turtle, snake, robin, rabbit, mouse, or human being. Most species on mammals have a tendency to get into the ears. On man they run over the skin or through the meshes of clothing, most commonly coming to rest about the garters or belt.

Of the hundreds of species in over thirty genera which are found in all parts of the world, fortunately only a few are willing to engorge on man, and only one very small group of closely related species in the genus *Trombicula*, called the tsutsugamushi group after the Japanese name of the disease, seem to be concerned with transmission of scrub typhus to man.

The only species commonly attacking human beings in North America are *Eutrombicula alfreddugési*, widely distributed in southern United States and in the Mississippi valley; *E. splendens* (= *masoni*), common in wet localities in the southeastern states; and *E. batatas* (= *Acariscus hominis*), a pest species widely distributed from the Gulf States and California to northern South America. In Europe *Neotrombicula autumnalis* is an annoying human pest. All parts of the Far East, New Guinea, and Australia have species which can make life miserable for man; two of the commonest in the area are *Trombicula hirsti* and *T. wichmanni*, which, according to Wharton, are very closely related to the pest species of the United States. These, however, are not the

transmitters of scrub typhus (see next section). In Queensland *T. sarcina* attacks man and also produces acute irritation and nasty sores on the legs of sheep. In Texas and the southeastern states a species of *Euschöngastia* is a pest of chickens and birds but leaves man alone.

The common pest redbug of the United States, *E. alfreddugési*, attacks principally turtles, snakes, ground birds, and rabbits and is content to feed on man and domestic animals, but unlike many species it does not often attack rodents. On snakes and lizards it may be so abundant as to form rusty red patches between the scales. This redbug is particularly abundant on loam or sandy soil covered by thickets but is seldom found in hardwood forests. Williams (1946) found them spottily distributed and especially abundant under blackberry bushes or at the base of trees. Before attachment they run about actively on or near the ground, eager to climb on a host, but they do not climb upon grass or brush. They can run about a foot in a minute—1500 times their own length—but ordinarily do not travel far.

The irritation caused by redbugs, as in other arthropod attacks, is largely due to sensitization to the saliva injected. The reaction reaches its height of itching in 12 to 24 hours, when the stylostome is well developed. Eventually the reaction becomes so rapid that very little saliva gets into the skin and the mites are unable to engorge; in some individuals almost complete immunity develops, except for a few reactive bites early in the season which act like a booster shot of a vaccine to revive immunity. Alcohol or camphor helps to allay the itching, and a bath with baking soda or ammonia in the water gives some relief, especially if taken soon after exposure. Dusting sulfur inside the stockings and on the legs is undoubtedly a helpful prophylactic if better repellents are not available (see below).

Transmission of Scrub Typhus. As mentioned previously a small group of closely related species of the genus *Trombicula* in the Far East are transmitters of scrub typhus, a rickettsial disease (see p. 229). *T. akamushi* (= *T. fletcheri*) in Japan and New Guinea and *T. deliensis*, probably only a subspecies, in a wide area from India to southwest China, Malaya, the East Indies, New Guinea, and Australia are the only proved transmitters. They are primarily parasites of rats, field mice (*Microtus*), shrews, and other mammals. Other species of trombiculids may spread infection among rodents, and in some places are suspected of transmission to man (Philip and Kohls, 1948). Field mice, rats, and shrews have been found naturally infected with the *Rickettsia* (*R. tsutsugamushi*) of scrub typhus and may serve as transient reservoirs, although the mites themselves are undoubtedly the principal reservoirs since they pass the organisms transovarially to

their offspring generation after generation. Since the mites normally attack only one host in the larval stage and are not parasitic at all in their later stages, transovarial transmission is a *necessary* feature in the epidemiology of this disease.

A *Rickettsia* similar to *R. conorii* of boutonneuse fever (see p. 569), and similar to one isolated from man in Belgian Congo, was isolated from trombiculid larvae taken from small mammals in tropical Africa. A rickettsia-like organism was also found in meadow mice (*Microtus*) on an island in the St. Lawrence River, where it is probably transmitted by larvae of *Trombicula microti*. Another redbug, *Schöngastia indica*, a very common parasite of rats in Java, has been found naturally infected with the *Rickettsia* (*R. mooseri*) of murine typhus, which is usually transmitted by fleas but *may* be transmitted by a bloodsucking mite, *Bdellonyssus bacoti* (see p. 538).

Scrub typhus usually begins with a black sore or "eschar" at the site of the infective bite. Fever, insomnia, generalized inflammation of lymph glands, aches, and neuritis are the usual symptoms; often there is a rash also. The mortality varies from 3 to over 50 per cent in different places. The disease is differentiated from "shop typhus" (endemic or murine typhus) by the OXK Weil Felix reaction. Treatment of this and other rickettsial diseases is discussed on p. 229.

Protection against Redbugs. Practically complete protection against redbugs and scrub typhus can be obtained for weeks by rubbing dibutyl phthalate into the clothing. Later benzyl benzoate was adopted, or a 50-50 mixture of the two. Other effective repellents are discussed on p. 519. Spraying local areas with DDT or preferably BHC in fuel oil or dust gave protection to troop encampments in infected areas in the Pacific theater during World War II, but Chlor-dane and Toxaphene have since proved to be better. These chemicals applied as dusts at only 2 lb. per acre have given 90 per cent control for 7 weeks.

Bloodsucking Mites (Dermanyssidae)

The suborder Mesostigmata (see p. 524) contains several families of bloodsucking mites. The families Dermanyssidae and Laelaptidae contain species that live in the nests and burrows of birds, rodents, etc., feeding on them while they are "at home" or sitting on nests. Important species from the human standpoint are certain species in the family Dermanyssidae: *Dermanyssus gallinae* of chickens and other birds, *Allodermomyssus sanguineus* of mice and sometimes rats, and *Bdellonyssus bacoti* of rats. Other species of *Bdellonyssus* parasitic on birds, especially *B. bursa* of poultry in the tropics, and *B. sylviarum*

of many wild birds, may be of importance as reservoirs of encephalitis viruses (see p. 734). Members of the related family Gamasidae are able to transmit tularemia to rodents by their bites.

***Dermanyssus gallinae*.** This, the "red mite" of poultry (Fig. 160A), along with one or two other species of poultry mites belonging to the family Dermanyssidae, often causes irritation and annoyance to

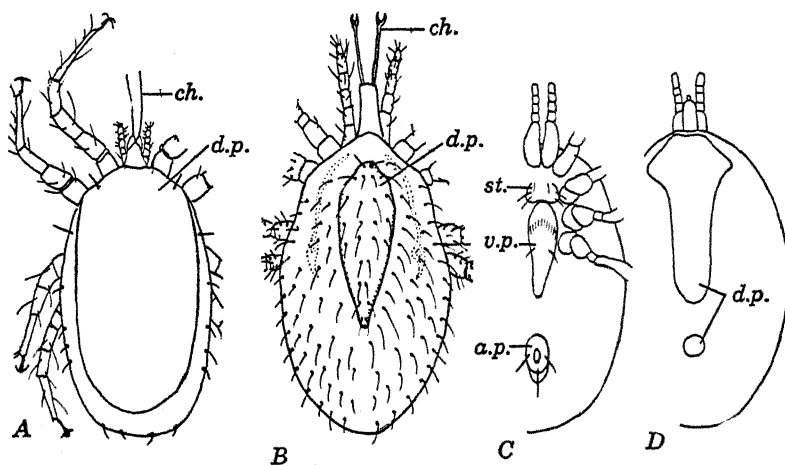


FIG. 160. Dermanyssid mites. A, *Dermanyssus gallinae*; B, *Bdellonyssus bacoti*; C, D, *Allodermanyssus sanguineus*, ventral and dorsal. Abbreviations: ch., chelicerae, needle-like in *Dermanyssus*, pincer-like in *Bdellonyssus*; d.p., dorsal plate, large in *Dermanyssus*, narrow in *Bdellonyssus*, and divided in *Allodermanyssus*; a.p., anal plate; v.p., ventral plate; st., sternal plate. (Adapted from various authors.)

people who work in chicken houses, live poultry markets, etc. Mites of this genus have a large dorsal shield rounded posteriorly (Fig. 160) and chelicerae that are needle-like in females but have pincer-like tips in males.

These mites live like bedbugs in cracks and crevices, nests, etc., feeding on the chickens mainly at night and sometimes doing much damage to them; they may actually bleed them to death. The eggs are laid in crevices and debris, and the larvae molt into eight-legged nymphs before they begin sucking blood. Although only able to live and multiply on birds, they may remain on human skin for a day or two, causing annoying bites. There is a report of a London hospital which was literally dusted with these mites originating from pigeon nests in the roof. Infested chicken houses, dovecotes, live poultry markets, etc., sometimes remain infested for several weeks after the birds have been removed.

This mite has been found to harbor and transovarially transmit the encephalomyelitis viruses of the St. Louis and western equine types. Many chickens develop antibodies, and the mites were suspected of being important reservoirs of these viruses in winter and between epidemics. It was further shown that *Bdellonyssus sylviarum* (see below) of wild birds sometimes harbors these viruses, and an interesting epidemiological situation was visualized—the virus harbored by mites which transovarially transmit them, and infect their bird hosts; the bird hosts bitten in summer by mosquitoes, which then pass the viruses on to horses, whence other mosquitoes transmit them to other horses and to man. Later work, however, casts some doubt on this matter (see Eklund, 1954).

Spraying with carbolineum or creosote was the time-honored method of getting rid of these chicken mites until the chlorinated hydrocarbons were developed (see p. 514). These chemicals have the advantage of not giving eggs flavors that did not come from the chickens.

***Bdellonyssus*.** Members of this genus are important parasites of birds and rats and are concerned in transmission of certain rickettsial and virus diseases. There are two nymphal stages, but the second nymphal stage does not feed. These mites have narrow dorsal shields, narrowed posteriorly (Fig. 160), and chelicerae that end in pincers in both sexes. *B. bacoti* (Fig. 160B), a common mite of rats in southern United States and throughout the tropics, is capable of transmitting endemic typhus (see p. 229) among rats and possibly occasionally to man, since it temporarily becomes an annoying human pest in rat-infested buildings when its normal hosts are killed or driven off. This mite is also able to transmit rickettsialpox (see next section) and Q fever (see p. 574). This mite should be distinguished from another common rat mite, *Echinolaelaps echidninus*, which has numerous conspicuous ventral plates and has not been incriminated as a disease carrier.

B. sylviarum is a frequent parasite of chickens and of many wild birds in North America and Europe, and *B. bursa* is an important chicken parasite in the tropics. *B. sylviarum*, as noted above, may be concerned in the epidemiology of encephalomyelitis viruses. Unlike *D. gallinae*, *B. sylviarum* stays on the feathers of the birds instead of retiring to crevices in chicken houses or nests, so it cannot be controlled by the same methods; this and other feather mites, as well as bird lice, can be controlled by spraying with lindane or chlordane.

Mites and Rickettsialpox. In 1946 an outbreak of this previously unknown rickettsial disease which occurred in New York City was traced to an infection in mice, transmitted by a mouse mite of this family, *Allodermanyssus sanguineus*. Subsequently this disease was

reported in other eastern cities. *A. sanguineus* has a divided dorsal shield (Fig. 160C, D). There are two nymphal stages in the life cycle, both of which feed. *Bdellonyssus bacoti* is also a potential vector of rickettsialpox. The disease begins like scrub typhus with a black eschar at the site of the bite, followed a week later by a sudden fever and a rash resembling chickenpox. The *Rickettsia* was named *R. akari* and is antigenically close to spotted fever.

Mites in the Lungs, Intestine, Urinary Passages, etc.

Lung Mites. As noted on p. 524, a number of mites live in the nose or lungs of snakes, birds, seals, and monkeys, but no true lung mites have been found in man. In Ceylon a number of cases of invasion of human lungs by normally free-living or plant-parasitic mites have been reported, accompanied by bronchial asthma and eosinophilia.

Mites in the Intestine. There have been numerous reports of intestinal infections with mites. The mites concerned have always been common household species of the families Acaridae (=Tyroglyphidae) or Glycyphagidae (grain and cheese mites, see p. 540), and Tarsonematidae, which also infest various vegetable products. The eggs and the mites in all stages of development are frequently found in the feces of man, and of dogs and other animals fed on mite-infested food, but they are always dead. This pseudoparasitism with mites sometimes fills unsuspecting technicians with wonder and excitement when they discover the large eggs in the feces.

It is possible that ingestion of the mites in considerable numbers may occasionally cause gastro-intestinal disturbances. Hase (1929) describes a famous German cheese, Altenburger "milbenkäse," that owes its piquant flavor to the presence of myriads of acarid mites, with which it is deliberately inoculated. The mites and their feces make a moving grayish powder on the surface. The ingestion of thousands of mites and their excretions with this cheese often causes gastro-intestinal disturbances when the cheese is eaten for the first time, but those used to it suffer no ill effects. Nevertheless, Hase observed that mite dust (dead mites, feces, cast skins, etc.) was so toxic to mice that 7 out of 12 fed with it died with dysenteric symptoms. The writer has seen dogs relieved of diarrhea when taken off mite-infested food. There is no doubt, however, that any ordinary contamination of human food with mites would be of no consequence, and there is no sound evidence that they ever become established in the alimentary canal.

Urinary Infections. Urinary infections with mites have frequently been reported, but in most of these cases it seems likely that the mites

observed are really contaminations from containers or other sources. However, there are a number of apparently *bona fide* infestations of the urinary tract in which no source of contamination could be found. Mackenzie and Mekie in 1926 reported finding mites in the urine of patients with uncontrollable nocturnal enuresis; the urine contained abundant epithelial cells, parts of mites, and a black deposit. The mites concerned were a tarsonematid, *Tarsonemus floricolus*, and acarids. The latter are found in sugar, cereals, etc., but the *Tarsonemus* ordinarily lives on plants. How they found their way into the urinary passages, if they actually did, is hard to understand. Another case is reported of dead mites being found day after day in the urine of a Japanese with cystitis. The mites, named *Nephrophages sanguinarius*, are believed to have been tarsonematids.

In rare instances acarid mites establish residence in the canal of the outer ear and occasionally even penetrate to the middle ear and mastoid.

There have been a number of reports of acarid mites being found in cancers and other situations in the tissues of the body, but it is practically certain that these are cases of contamination.

Grocer's Itch and Allied Forms of Mite Dermatitis

Grain Mites. Many mites, most of them belonging to the families Acaridae (=Tyroglyphidae) and Glycyphagidae, are common pests of human dwellings, stores, and warehouses, where they attack all sorts of food materials, stored seeds, stuffing of furniture, etc. When conditions are favorable they multiply until the infested materials are literally alive with them. They are especially commonly found in animal feeds, hay, grain, flour, sugar, dried fruits, copra, cottonseed, and cheese.

People who come into close association with infested goods develop symptoms which Hase (1929) thinks are of allergic nature. Though allergy undoubtedly plays a part, there is evidence that the bodies or excretions of the mites are toxic; this was shown by Hase's feeding of mite dust to mice (see previous section). The occurrence of purely allergic responses is not so common as to account for the appearance of dermatitis in whole groups of people working with infested materials, e.g., copra workers, or of all the people in a neighborhood acquiring dermatitis from dust from a grain elevator (see p. 543). It is true, however, that contact with living mites is unnecessary; symptoms are produced as readily, if not more so, by rubbing infested material on the skin, by having dust from it blow on the skin, or even by breathing the dust.

Both dermal and respiratory symptoms occur. The skin develops

a typical itching urticaria, sometimes with large hives, sometimes eczematous. Asthma is common, and other frequent symptoms are quickened pulse, general aches, fever, and sometimes nausea, vomiting, and diarrhea. It is obvious that these symptoms are by no means peculiar to mite infections but are frequently observed in severe arthropod infections of other kinds. Few arthropods except mites develop in sufficiently prodigious numbers in human habitations to produce symptoms by their dust; in almost all other cases—bedbugs, fleas, mosquitoes, ticks, etc.—the production of symptoms depends upon the inoculation of saliva at the time of biting.



FIG. 161. Left, grain mite, *Tyrophagus putrescentiae* (= *Tyroglyphus longior*), $\times 30$. (After Fumonze and Robin.) Right, hypopus or traveling stage, ventral view. Much enlarged. (After Banks, *U.S. Dept. Agric. Repts.*, 108.)

Some of the well-known examples of dermatitis from mites are grocer's or baker's itch, known all over the world; "copra itch" in copra mills in Ceylon; "miller's itch," familiar in most grain-raising countries; "vanillism" in handlers of vanilla pods; "cottonseed itch"; "barley itch"; etc. The affliction is not confined to man, for horses sometimes get dermatitis when provided with mite-infested hay.

Grain mites are small white or yellowish, soft-bodied mites. They have prominent pincer-like chelicerae which are entirely unsuited for piercing the skin. The three commonest genera are *Acarus* (= *Tyroglyphus*), *Tyrophagus* (Fig. 161), and *Glycyphagus*. The first two have elongate bodies, with a suture separating the body into anterior and posterior parts, and with a few long simple hairs; *Glycyphagus* is squattier, with a finely granulated back, finely feathered hairs, and no body suture.

The life cycle of many species is remarkable in that, after reaching a nymphal stage in orthodox mite style, the mites change into a form called a hypopus (Fig. 161, right), which is a special adaptation for hitchhiking. There are no mouth parts, the legs are short and stumpy,

and there are ventral suckers on the abdomen. In some species an encysted type of hypopus is produced to withstand desiccation. Thus equipped for travel, the mites attach themselves to insects or other objects and are transported to new localities. They have frequently been mistaken for parasites, but they are no more parasitic than a man on horseback. After dropping from their animated conveyances they molt into eight-legged nymphs, which after feeding become adults.

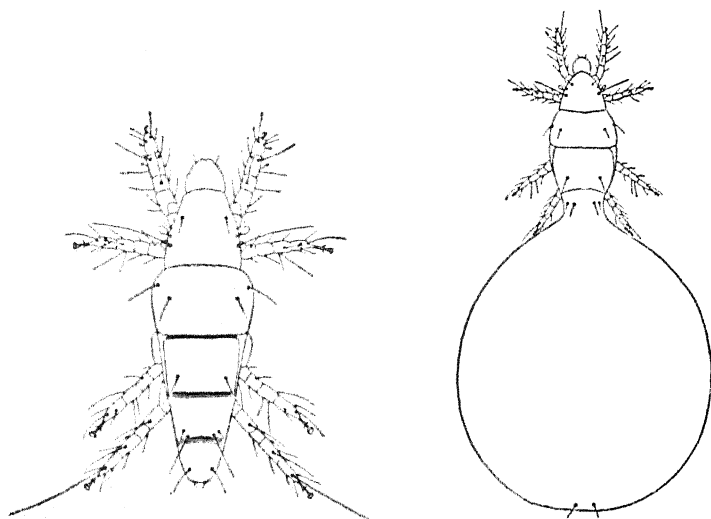


FIG. 162. *Pyemotes* (= *Pediculoides*) *ventricosus*. Left, virgin ♀. Right, partially gravid ♀. In fully gravid females the abdomen swells to several times the size shown here. (From Baker and Wharton, *Acarology*, Macmillan, 1952.)

Infested substances are best burned or otherwise disposed of, and the containers, rooms, etc., then fumigated, preferably with methyl bromide (see p. 226). Carbon dioxide snow added to grain or feed in containers is often helpful in keeping down mites as well as mealworms and weevils.

***Pyemotes ventricosus*.** This mite (Fig. 162), formerly called *Pediculoides ventricosus*, belongs to the family Pyemotidae and is related to the Tarsonematidae (see p. 524). The males and unencumbered females are only about 0.2 mm. long, barely visible to the naked eye. The pregnant females, however, retain their eggs and young in the abdomen until they are fully developed, the abdomen becoming a grotesquely enlarged brood sac, which may reach a diameter of 1.5 mm. The females retain their slender virginal form very briefly, for

it may be only 6 days from the time they leave their distorted mother until they have a sacful of young of their own.

These mites are normally parasitic on grain-moth caterpillars and other insects in straw, grains, cottonseed, etc. In stored products the transformation and escape of their insect prey leave them with their normal food supply cut off, and the hungry and thirsty mites then attack any flesh that comes their way. Serious infestations occur among grain thrashers, millers, etc., and sometimes new straw mattresses turn out to be veritable beds of fire.

An itching rash begins about 12 to 16 hours or sooner after exposure to the mites. The bites, at first red and inflamed, itch unbearably. Little blisters form and, when scratched and ruptured, develop into pustules or scabs; in bad attacks the usual constitutional symptoms of severe arthropod infestation develop—fever, rapid pulse, headache, nausea, etc. One case has been reported in which dust from a mite-infested grain elevator blew into the cottages in the neighborhood and produced dermatitis in all the inhabitants. Since the mites cannot thrive on human blood they soon withdraw, disillusioned, to try some other source of food, and consequently the symptoms usually subside within a week unless fresh detachments of mites are constantly being acquired.

The itching can be alleviated by alkaline baths or application of soda and soothing ointments. People exposed to infestation can get protection from bites by application of ointments or sulfur, followed by a change of clothes and a bath after exposure, but those who develop a dust dermatitis will get little relief from these measures.

Other Dermatitis-Producing Mites. A number of other mites may occasionally produce dermatitis. Brief mention should be made of members of the family Cheyletidae, belonging to the Trombidiformes, which prey on truly parasitic mites in the fur or plumage of animals. One species, *Cheyletiella parasitivorax*, often found on rabbits and cats, occasionally attacks the mammalian host. This mite has been found responsible in a few cases of human eczema from handling cats.

Oribatids

The oribatid mites (see Fig. 107) are free-living mites living in soil, moss, etc., feeding on molds and organic debris. They are very numerous and probably important, as are earthworms, in connection with soil fertility. They are of interest to parasitologists because many species, belonging to a number of different families, serve as intermediate hosts of tapeworms of the family Anoplocephalidae (see p. 366). They creep out of the soil when the dew is on the grass, and are eaten

by herbivorous animals with the vegetation. The principal factors determining their importance as tapeworm vectors are their abundance where the hosts of the tapeworms feed and their ability to swallow the tapeworm eggs.

THE PENTASTOMIDA

Tongue Worms and Their Allies

At one time this aberrant group of arthropods was classified with the Arachnida and was thought to be related to the mites, but it is now usually considered a separate class. The animals have become so modified by parasitic life that their affinity with the arthropods would be difficult to recognize if it were not for the form of the larvae, which are more or less mite-like and have either two or three pairs of legs. Even in life cycle they resemble parasitic worms in that they pass the immature stages in an intermediate host.



FIG. 163. Left, head of *Armillifer armillatus*, $\times 3$ (after Sambon, *J. Trop. Med. Hyg.*, 25, 1922). Right, head of nymph of *Linguatula serrata*, $\times 25$ (after Faust, *Am. J. Trop. Med.*, 7, 1927).

The adults have elongate bodies which are either flattened or cylindrical and divided into a series of unusually conspicuous rings which are not, however, true segments. There is no distinct division into head, thorax, or abdomen. On either side of the mouth at the anterior end there are two pairs of hollow, fang-like hooks, in some forms situated on finger-like parapodia, which can be retracted into grooves like the claws of a cat (Fig. 163). These are believed to be vestiges of some of the appendages. At the bases of the retractile hooks there open a number of large glands, the secretion of which is believed to be hemolytic. The Pentastomida have a simple nervous system, a usually straight digestive tract, and a reproductive system. The anus is at the posterior end of the body. The females, which are larger than the males, have the genital opening either near the anterior or near the posterior end of the abdomen, but that of the males is anterior.

The life cycle involves two hosts. The adults usually live in the lungs or air passages of their hosts; the larvae live free or encysted in the viscera of some other host.

Classification. The classification of the Pentastomida according to Heymons and Vitzthum (1936) is as follows:

Order 1. **Cephalobaenida.** Hooks situated on finger-like processes or at least swellings of the body behind mouth; genital opening anterior in both sexes.

Family 1. **Cephalobaenidae.** In lungs of lizards and snakes.

Family 2. **Reighardiidae.** In air sacs of gulls and terns.

Order 2. **Porocephalida.** Hooks not on prominences, arranged trapeze-like or in a curved line on either side of mouth; ♀ genital opening posterior.

Family 1. **Porocephalidae.** Body cylindrical. Adults in lungs of reptiles, young in a great variety of vertebrates; young of the genus *Armillifer* usually in mammals, including man.

Family 2. **Linguatulidae.** Body flattened. Adults in nasal passages of dog and cat family, except one in crocodiles; young in all sorts of mammals, including man.

There is a single well-authenticated instance of human infection with an adult *Linguatula serrata* in the nasal passages, but visceral infection with immature stages of this species and of several species of Porocephalidae is surprisingly common.

Linguatula serrata. The adult worms are nearly colorless; the females are 100 to 130 mm. long with a maximum width of about 10 mm.; the males are only about 20 mm. long and 3 to 4 mm. wide. They occur in the nasal passages and frontal sinuses principally of dogs (Fig. 164A, F) and occasionally other animals, where they suck blood. They sometimes cause severe catarrh, bleeding, and suppuration and may cause much sneezing and difficulty in breathing when they obstruct the nasal passages, but often they produce no symptoms at all.

The eggs (Fig. 164B), containing embryos with four rudimentary legs, are voided by the host with the catarrhal products of the respiratory system, the egg-laden mucus infecting water or vegetation. According to Hobmaier and Hobmaier (1940) eggs which are swallowed hatch, and the larvae enter the body cavity but fail to develop further in dogs or cats. The eggs are resistant and live for a long time outside the body. When ingested by an intermediate host, e.g., cattle, sheep, rabbits, rats, man, etc., the embryos (Fig. 164C), 75 μ long, migrate to the mesenteric nodes and various other viscera and there become encapsulated (Fig. 164D). They molt twice and assume a pupa-like stage in which they are devoid of mouth parts, hooks, or segmentation, and are 0.25 to 0.5 mm. long. A number of other molts follow, and after 5 or 6 months a nymphal stage is attained in which the animal possesses two pairs of hooks and has its body, 4 to 6 mm.

in length, divided into 80 to 90 rings, each bordered posteriorly by a row of closely set spines (Figs. 163, *right*, 164E). These are shed when the nymph transforms into an adult. For a long time this nymph was looked upon as a distinct species. The nymphs may remain alive

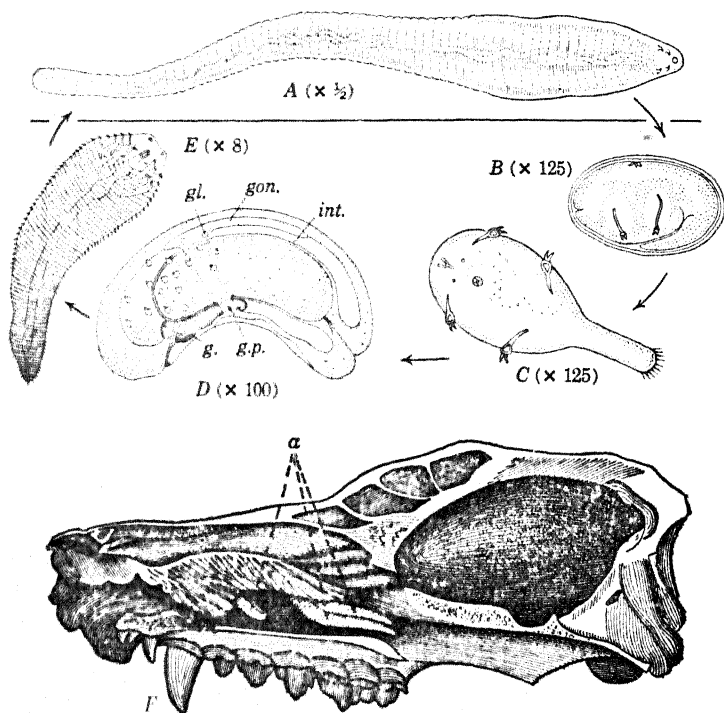


FIG. 164. *Linguatula serrata*, life cycle. A, adult ♀ from nasal passage of a dog; B, egg containing embryo; C, first-stage larva from viscera of sheep, man, etc.; D, third-stage larva, ninth week; E, nymph, from liver of sheep; F, head of dog split open to show three tongue worms, *Linguatula serrata*, (a) in nasal cavity. (A adapted from Brumpt, *Précis de parasitologie*, 1949. B-D, from Leuckart, *Bau und Entwicklungsgeschichte der Pentastomen*, 1860. E, from Railliet, *Recueil méd. vét.*, Alfort, 1884. F, after Colin, *Recueil méd. vét.*, 1863.)

in the intermediate host for at least 2 to 3 years, but their capsules become thick so that they are not easily liberated. This undoubtedly interferes with successful infection of a final host.

According to the Hobmaiers, contrary to the generally accepted belief, the nymphs do not leave their cysts during the life of the host but quickly liberate themselves after its death. Nor do swallowed nymphs succeed in migrating back to the pharynx from the stomach. To cause infection the nymphs must cling to the mucous membrane of the mouth

before being swallowed or when vomited. The worms begin laying eggs about 6 months after infection and seem to live for about 2 years.

L. serrata is nowhere abundant, even in its normal hosts, though it has a wide geographic distribution. In parts of Europe 10 per cent of dogs may harbor the adults, and in some series of autopsies 10 per cent of human beings may harbor the nymphs, but usually they are dead and calcified and of no pathological significance. In North Ireland the adults are frequent in foxes, and the nymphs in lymph nodes of cattle. Undoubtedly human infections result from too intimate contact with dogs. In the single human infection with the adult stage a frequent bleeding of the nose which had persisted for seven years ceased when an adult *Linguatula* was expelled in a violent fit of sneezing.

Armillifer. Man is frequently parasitized by the nymphs of at least two species of *Armillifer* (*Nettorhynchus*, according to Dollfus, 1950), the adults of which live in the lungs of pythons and other snakes. The intermediate hosts include many kinds of mammals but particularly monkeys, which are important in the diet of pythons. Human infections with the encysted larvae of *A. armillatus* are common in Africa; Broden and Rodhain found 30 cases in 133 post-mortems of natives in Belgian Congo. Since some African natives esteem python for dinner, infection may result from handling them, as well as from contaminated water or vegetables. In the Oriental region this species is replaced by a closely related one, *A. moniliformis*; only a few human infections with this species have been seen—in Manila, Sumatra, and China.

These species of *Armillifer* have bright lemon-yellow cylindrical bodies, marked by bracelet-like annulations which give them a screw-like appearance (Fig. 165A, B). The females are 90 to 130 mm. long, the males about 30 to 45 mm. In the intermediate hosts the nymphs lie coiled up in cysts either embedded in or attached to the liver or other organs; they resemble miniatures of the adults. When ingested by pythons they are said to reach the lungs by burrowing through the stomach wall, but this may be incorrect, since both *Porocephalus crotali* and *Linguatula* reach the lungs via the throat and trachea (Penn, 1942). In the intermediate host development is very slow, the nymphs requiring 1½ to 2 years to reach a length of 16 to 22 mm.

Two American cases of infection with porocephalid worms have been recorded. Since no American species of *Armillifer* are known, these worms may have been the young of *Porocephalus crotali* of rattlesnakes (Fig. 165D), or of *Kiricephalus coarctatus* of Colubridae (Fig. 165C). Both these genera although having annulated bodies lack the conspicuous rings of *Armillifer*. *P. crotali* nymphs are common in muskrats and other mammals.

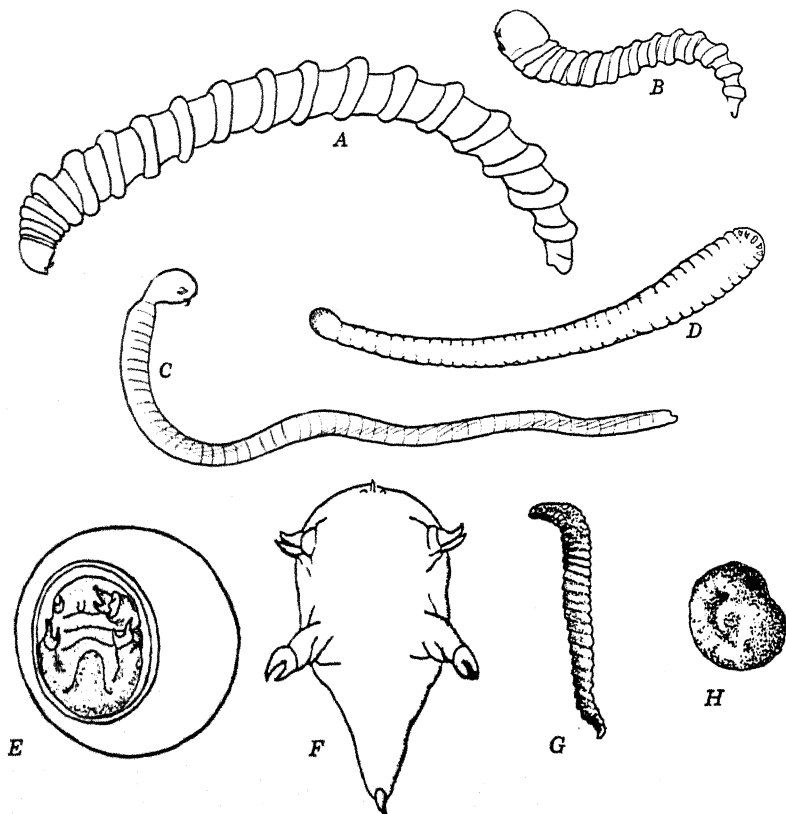


FIG. 165. A, *Armillifer armillatus* ♀; B, same, ♂; C, *Kiricephalus coarctatus*, common in American colubrine snakes; D, *Porocephalus crotali*, in American rattlesnakes. (A-C, E, F, adapted from Sambon, *J. Trop. Med. Hyg.*, 25, 1922. D, from Self and McMurray, *J. Parasitol.*, 34, 1948. G and H, from Fülleborn, *Arch. Schiffs- u. Tropen-Hyg.*, 23, 1919.)

Heavy experimental infections with immature worms produce injurious or even fatal effects, but there is no evidence that the light infections usually seen in man are pathogenic. One heavily loaded case reported by Cannon (1942) suffered from partial obstruction of the colon due to thickening of its parasite-studded walls. Since there are no characteristic symptoms, infections are recognized only at autopsies.

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Ticks

Although the ticks constitute only one of the suborders of the order Acarina, they are popularly regarded as a quite distinct group because they are large and easy to recognize. They are not merely annoying pests but surpass all other arthropods in the number and variety of disease agents for which they are carriers. As carriers of human disease they rank next to mosquitoes, but as carriers of animal diseases they are preeminent.

General Anatomy. The ticks are classed in two families, Argasidae or "soft" ticks, and Ixodidae or "hard" ticks, which differ considerably both in their structure and life cycle, as will be seen in the following pages. Structurally the Argasidae (Fig. 166E, F) are distinguished by having the body covered by a leathery cuticle marked by numerous tubercles or granulations, and sometimes small circular discs, also, but no plates or shields. The Ixodidae, on the other hand (Fig. 166A-D) have a dorsal shield or scutum that almost completely covers the back in males, but only the anterior portion of it in females. In some genera (*Dermacentor* and *Amblyomma*) the dorsal shield or scutum is ornamented with silvery markings and is then said to be "ornate" (Figs. 174, 176). In several genera the dorsal shield of the male is marked with "festoons" on the posterior border (Fig. 166A, B). Another character distinguishing these two families is the ventral position of the mouth parts in the Argasidae and their anterior position in the Ixodidae, where they fit into a groove or *camerostome* at the anterior end of the body. The females of both families when unfed are flat, but after their gluttonous meals they become grotesquely engorged and resemble beans or nuts (Fig. 168). The dorsal shield or scutum of engorged female ixodids becomes quite inconspicuous.

The mouth parts, as in other Acarina, are borne on a movable *capitulum* or *gnathosoma*, which is not a true head although popularly so called; it consists of a base (*basis capituli*) and the mouth parts (Fig. 167A, B). The latter consist of a *hypostome*, a pair of *palpi*, and a pair of mandibles or *chelicerae*. The hypostome is a prolonga-

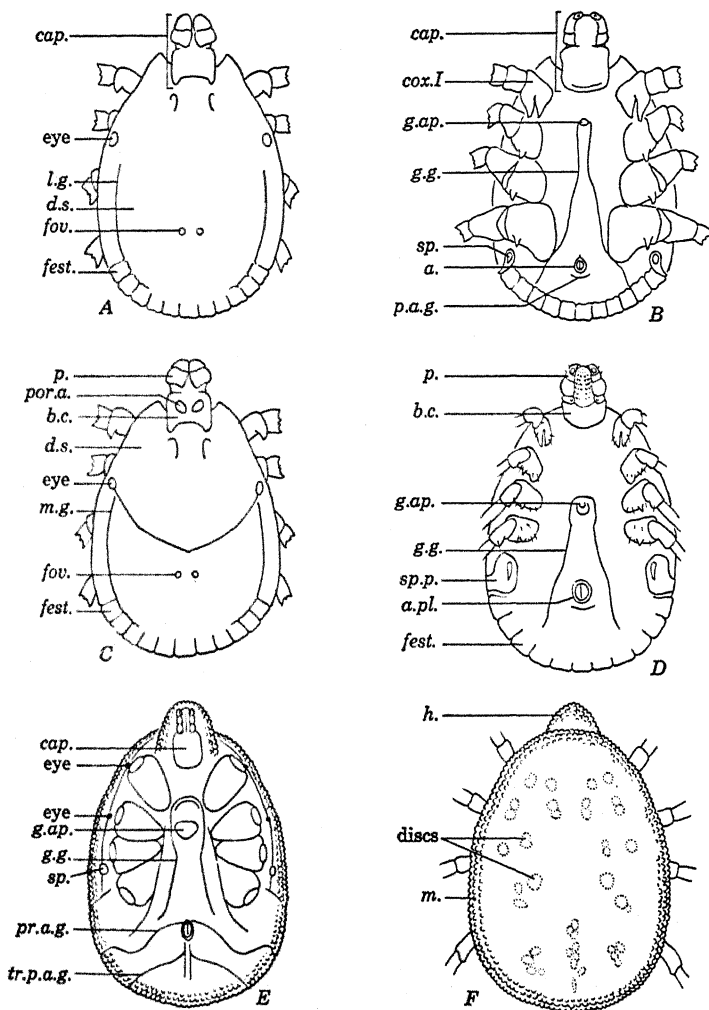


FIG. 166. Dorsal and ventral views of ixodid and argasid ticks. A and B of ♂ ixodid (*Dermacentor*); C and D of ♀ ixodid (*Dermacentor*); E and F of argasid (*Ornithodoros*). Abbreviations: *a.*, anus; *a.pl.*, anal plate; *b.c.*, basis capituli; *cap.*, capitulum; *cox.I*, first coxa; *d.s.*, dorsal scutum or shield; *fest.*, festoons; *fov.*, fovea; *g.ap.*, genital aperture; *g.g.*, genital groove; *h.*, hood; *l.g.*, lateral groove; *m.*, mammillae; *m.g.*, marginal groove; *p.*, palpus; *p.a.g.*, post-anal groove; *por.a.*, porose area; *pr.a.g.*, pre-anal groove; *sp.*, spiracle; *sp.p.*, spiracular plate. (Adapted from Cooley, *N.I.H. Bull.* 171, and Cooley and Kohls, *Am. Midland Nat.*, Monogr. 1, 1944.)

tion of the ventral wall of the capitulum. It is a formidable piercing organ beset with row after row of recurved teeth (Fig. 167C-K); these cause it to hold so firmly in the flesh into which it is inserted that forcible removal of the tick is liable to tear the body away from the capitulum,

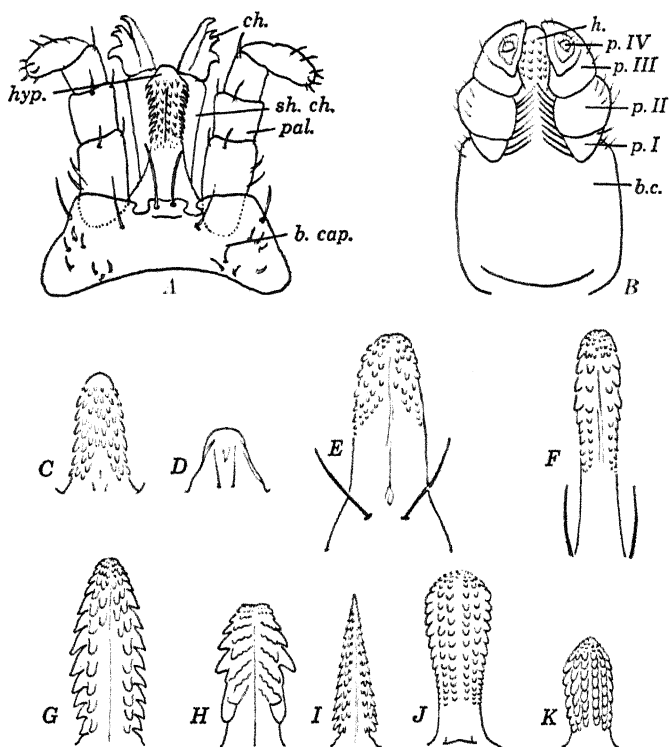


FIG. 167. A, capitulum of argasid tick, ventral view (from Matheson, *Medical Entomology*, Comstock). B, capitulum of ixodid tick (*Dermacentor*), ventral view (after Cooley, *N.J.H. Bull.* 171); b.c., b. cap., basis capituli; ch., chelicera; h., hyp., hypostome; pal., palpus; p.I-IV, palpal segments; sh. ch., sheath of chelicera. C-K, hypostomes of: C, *Otobius megnini*, nymph; D, same, adult; E, *Ornithodoros savignyi*, adult; F, *O. turicata* ♀; G, *Ixodes scapularis* ♀; H, same, ♂; I, *Ixodes mexicanus* ♀; J, *Rhipicephalus sanguineus* ♀; K, *Haemaphysalis leporis-palustris* ♀. (Sketched from various authors.)

which remains embedded in the skin. The chelicerae are elongate, slender structures lying above the hypostome; at the tip they have a movable articulated digit armed with teeth. The palpi are limber, leg-like structures in the Argasidae, but rigid and closely associated with the hypostome in the Ixodidae; in the latter the fourth segment is embedded in a pit on the ventral side of the third segment (Fig.

167*A, B*). The single pair of spiracles are situated on the sides of the body near the fourth coxae. The legs of all four pairs (three pairs in the larvae) are much alike and are terminated by a pair of claws on a stalk. The legs are long and conspicuous when the body is empty but are hardly noticeable after engorgement.

The genital aperture is situated on the ventral side between the first or second pair of legs, the anus about halfway between the fourth pair of legs and the hind margin of the body. The presence and position of grooves on the ventral side of both sexes and the presence or absence of ventral shields in male ixodids are characters of taxonomic value.

Habits and Life History. All ticks are parasitic during some part of their lives. The majority of them infest mammals, though many species attack birds and some are found on cold-blooded animals. A

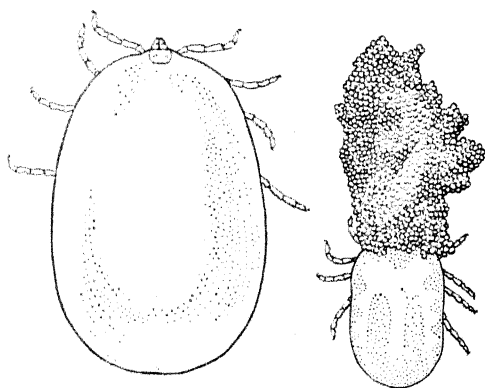


FIG. 168. Left, engorged tick (*Dermacentor*). Right, cattle tick, *Boophilus annulatus*, laying eggs (adapted from Graybill, *Farmer's Bull.*, 1912.)

decided host preference is shown by some species, whereas others, e.g., *Ixodes ricinus*, the European castor-bean tick, appear to be content with practically any bird or mammal that comes their way. For many species the hosts or parts of hosts differ in the different stages. Many ticks, including *I. ricinus*, attack birds more frequently as larvae or nymphs, and mainly mammals as adults; *Dermacentor* usually attack small rodents and rabbits (and some species of birds) in their immature stages and large mammals, including man, as adults.

According to Philip (1953) ticks are attracted by animal smells up to distances of at least 50 ft., and tend to collect along game trails. Ticks can be collected by dragging a muslin cloth over infested vegetation or ground.

The life histories of argasid and ixodid ticks differ principally in that the Argasidae, like most arthropods, feed repeatedly as adults and lay eggs in batches of 20 to 250 after each gluttonous meal. Ixodid adult females, however, take a single enormous meal, after which they drop off the host and lay all their eggs at once, from several hundred for some species to upwards of 18,000 for others, piling them up in elongate masses in front of them (Fig. 168, *right*). Few if any insects are as prolific as that. The process of converting the engorged blood into eggs and depositing them occupies several days.

The eggs develop after an incubation period which varies with the temperature from 2 or 3 weeks to several months. Eggs deposited in the fall do not hatch until the following spring. Newly hatched ticks are called larvae or "seed ticks" and are recognizable by having only six legs (Fig. 175*B*).

In the Ixodidae the seed ticks assume a policy of watchful waiting until some suitable host passes within reach; often they crawl up on a blade of grass or a twig to reach a strategic position. Seed ticks must be imbued with almost unlimited patience, since in many if not in the majority of cases long delays must fall to their lot before a suitable host comes their way, like a rescue ship to a stranded mariner. The larvae of some species survive unfed for a year or longer. The jarring of a footstep or rustle of bushes causes the ticks instantly to stretch out to full length, feeling with their clawed front legs, eager with the excitement of a life or death chance to be saved from starvation.

If success rewards their patience, even though it may be after many days or weeks, they feed for only a few days, becoming distended with blood and then dropping to the ground again. Retiring to a concealed place they rest for a week or more while they undergo internal reorganization. Finally they shed their skins and emerge as eight-legged but sexually immature ticks known as nymphs (Fig. 175*C*), distinguishable from females by absence of the genital aperture and of porose areas on the basis capituli (Figs. 166*C*, 169). The nymphs climb up on bushes or weeds and again there is a period of patient waiting, resulting either in starvation or a second period of feasting. Once more the ticks drop to the ground to rest, transform, and molt, this time becoming fully adult and sexually mature. In this condition a host is awaited for a third and last time, and if again successful the females search for mates, copulate, and begin on their final engorgement, which results in distending them out of all proportion. Some ixodid females commence feeding before mating, but fill up more rapidly after mating. Some species of *Ixodes* which live on hosts with

fixed lairs copulate before finding a host, and in such species the male is often not parasitic at all and may differ markedly from the female in the reduced structure of its hypostome. The males usually die shortly after copulation. Most ticks, it will be seen, spend more time off their hosts than on; *Ixodes ricinus* spends only about 3 weeks of its 3 years of life on its hosts.

This, in general, is the life history of ixodid ticks, but it is subject to considerable variation in different species. In many species there are two nymphal periods instead of one. In some species, as in the cattle tick, *Boophilus annulatus*, both molts take place directly on the host, thus doing away with the great risk of the tick's being unable to find a new host after each successive molt. In a few species the first molting period is passed on the host, but the second is passed on the ground. According to the number of times ticks risk their future by leaving their hosts to molt and then seeking new hosts, they are called one-host, two-host, or three-host ticks. The majority of species have not yet discovered the advantage of molting on the host. The most important asset of ticks to counterbalance the disadvantage of having to find new hosts is their extraordinary longevity. Larvae of ticks, as noted above, may live a year or more without food, and adults have been kept alive in corked vials for 5 years.

The Argasidae differ in that they inhabit the nests or burrows of their hosts instead of the host itself. They usually drop off a host soon after a meal, which in different species takes 10 minutes to several days, so they are seldom carried away from the abode of the host. This is in contrast to the Ixodidae, which inhabit the hosts rather than the homes and frequently remain attached for several days or even longer. Female Argasidae, except *Otobius*, lay batches of eggs at intervals of 2 to 4 months, the first laying beginning a week to several months after mating and feeding. The eggs may number hundreds instead of thousands—a safe condition since the young argasids, reared in the home of the host, are in a much more advantageous position than the progeny of Ixodidae, which drop off and deposit their eggs anywhere in the wanderings of their host.

The Argasidae lead more regular and less precarious lives. Some species may feed several times between molts and may molt two to five times as nymphs. A few fail to feed in the larval stage at all, becoming nymphs about hatching time. *Otobius* does its last engorging as a second-stage nymph; the adults are not parasitic and have a toothless hypostome (Fig. 167D). The minimum time required to reach the adult stage varies from 3 to 12 months in different species. Adults may survive 5 to 12 years, including several years of starvation.

Classification, and Important Species

Classification. Both Argasidae and Ixodidae contain numerous disease transmitters and many others that are troublesome on account of the painfulness or subsequent effects of their bites. The family Argasidae contains four genera, *Argas*, *Ornithodoros*, *Otobius*, and *Antricola*, whereas in the Ixodidae there are about a dozen genera and about 400 species. The following table gives the principal distinguishing characters of the genera which are of interest as parasites of man or domestic animals. As will be seen, the important differentiating characters are the nature of the cuticle, presence or absence and number of anal plates in the male, details of the capitulum, and presence or absence of festoons and silvery ornamentation.

Argasidae. No dorsal shield, capitulum ventral.

1. Dorsal and ventral surfaces demarcated by a marginal line; cuticle with small circular discs but without distinct protuberances (Fig. 170A,C) *Argas*.
2. Margins of body not clearly demarcated or differentiated; cuticle warty, with ridges or other types of distinct protuberances (Figs. 170D, 171, 173) *Ornithodoros*.
3. Same as *Ornithodoros* but body of nymphs spiny; adults not parasitic (Fig. 171D) *Otobius*.

Ixodidae. Dorsal shield present; capitulum anterior; inhabit hosts, feeding once between molts. (See Figs. 166, 169.)

- 1a. Anal groove in front of anus, horseshoe-like; scutum inornate; abdomen not festooned; long mouth parts; no eyes; male with many ventral plates *Ixodes*.
- 1b. Anal groove behind anus or absent 2.
- 2a. Palpi longer than width of capitulum 3.
- 2b. Palpi shorter than width of capitulum 4.
- 3a. Second and third joints of palpi almost equal; male with adanal and a pair of accessory shields, festoons usually present *Hyalomma*.
- 3b. Second joint of palpi elongated; scutum ornate; abdomen festooned; male without adanal shields; only distal half of hypostome toothed *Amblyomma*.
- 4a. Anal groove absent or very indistinct; no festoons; male with 2 pairs of ventral shields *Boophilus*.
- 4b. Anal groove distinct; festoons present 5.
- 5a. Ornate; first coxa deeply cleft (Fig. 172); basis capituli rectangular; second joint of palpi longer than third; male without ventral shields, but with festoons *Dermacentor*.
- 5b. Inornate 6.
- 6a. Palpi conical, second joint flaring at base; basis capituli rectangular; first coxa not deeply cleft; male without ventral shields *Haemaphysalis*.
- 6b. Palpi not conical, 2nd and 3rd segments of palpi about equal; basis capituli pointed at sides; first coxa deeply cleft, male with one pair of ventral shields *Rhipicephalus*.

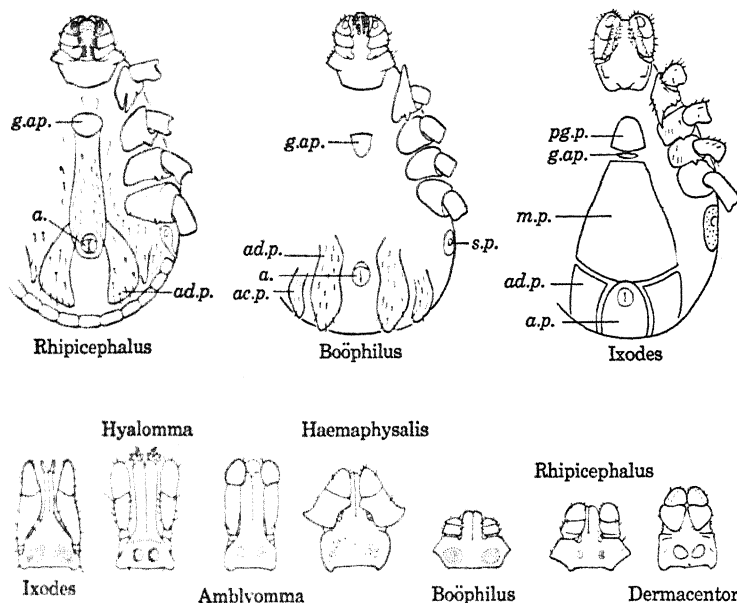


FIG. 169. Upper figures, ventral views of ♂, showing ventral plates; a., anus; ac.p., accessory plate; ad.p., adanal plate; g.ap., genital aperture; m.p., median plate; pg.p., pregenital plate; sp., spiracle. Lower figures, capituli characteristic of various genera; note porose areas on bases capituli. (Adapted from various authors.)

Important Species and Genera of Argasidae. In the family Argasidae the genus *Argas* is more common on birds than on mammals. *Argas persicus* (Fig. 170) is an important pest of poultry in all warm parts of the world, and transmits fowl relapsing fever and probably "range paralysis." In Iran, where it is called the "Miana bug," it frequently invades houses and attacks man, causing painful bites. *Argas reflexus* is an important parasite of pigeons. In Europe people may suffer severely from their attacks when they move into a house where pigeons were formerly kept, even if years ago, or if they dispose of birds that once shared a residence.

The genus *Otobius* contains only two species, the ear tick, *O. mégnini*, found in southwestern United States and Mexico, and a rabbit tick in the northwest. *O. mégnini* has habits unlike other argasid ticks in that the spiny nymphs (Fig. 171D) often remain attached to the ears of horses and other domestic animals, and sometimes children, for months. The adults are not parasitic and do not feed.

The members of the genus *Ornithodoros*, about fifty in number, attack mammals primarily. Some species live almost entirely on rodents and

other small mammals, some attacking man and domestic animals much more readily than others. There are about a dozen species that confine their attentions to bats. *O. moubata* (Fig. 173) in Africa habitually lives like the bedbug in human habitations, and rarely bites any animals but man, pigs, and warthogs. A number of other species invade houses, trailing along with rats or other animals, and then may bite the human inhabitants. A species occasionally found in houses in northern United States is a bat tick, *O. kelleyi*.

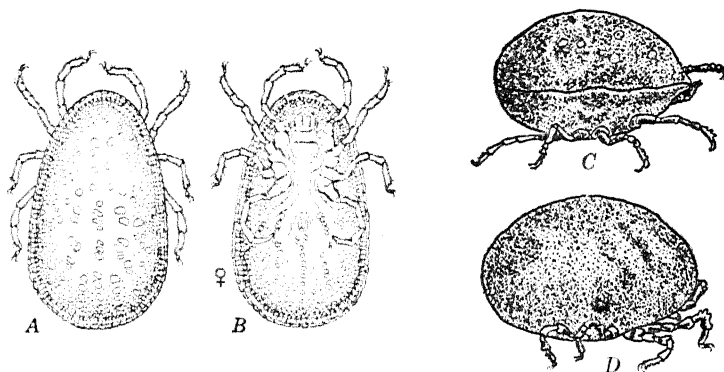


FIG. 170. A and B, *Argas persicus*, fowl tick, dorsal and ventral views of ♀. C and D, side views of engorged *Argas* and *Ornithodoros*, respectively, showing demarcation between dorsal and ventral parts of body (sutural line) in former, absent in latter.

Some species of *Ornithodoros*, e.g., *O. coriaceus* of California, cause painful and serious bites, but these ticks are particularly important as transmitters of relapsing fever (see p. 566). *Ornithodoros* ticks can also harbor a number of other diseases, e.g., spotted fever, tick-bite fever, Q fever, tularemia, and Russian encephalitis. Some species, e.g., *parkeri*, *nicollei*, and *rudis*, can transmit spotted fever by their bites, and different ones (*moubata* and *hermsi*) can transmit Q fever. The species of importance in connection with relapsing fever are discussed further under "Ticks and Relapsing Fever." Since these ticks are so important as potential transmitters of relapsing fever all over western North America, from Mexico to British Columbia, a key for the identification of important American species is given here.

Key to Important American Species of *Ornithodoros*

- 1a. Two pairs of eyes present; first coxa distinctly separated from others (Fig. 171I, 171H); large irregular depressed areas on back lacking tubercles; ♀ up to 9 mm. long; Southern California and Mexico *coriaceus*.
- 1b. No eyes; first coxa barely, if at all, separated from others; small disc-like or irregular areas without tubercles; length of ♀ 5 to 7 mm. 2.

- 2a. A pair of movable cheeks (Fig. 171H) at sides of camerostome (*talaje* group) 3.
 2b. No movable cheeks at sides of camerostome 4.
 3a. Tubercles coarse; numerous irregular areas without tubercles (Fig. 171C); no marked distal hump on tarsus 1; Mexico and Central and South America, sporadic all over the United States *talaje*.

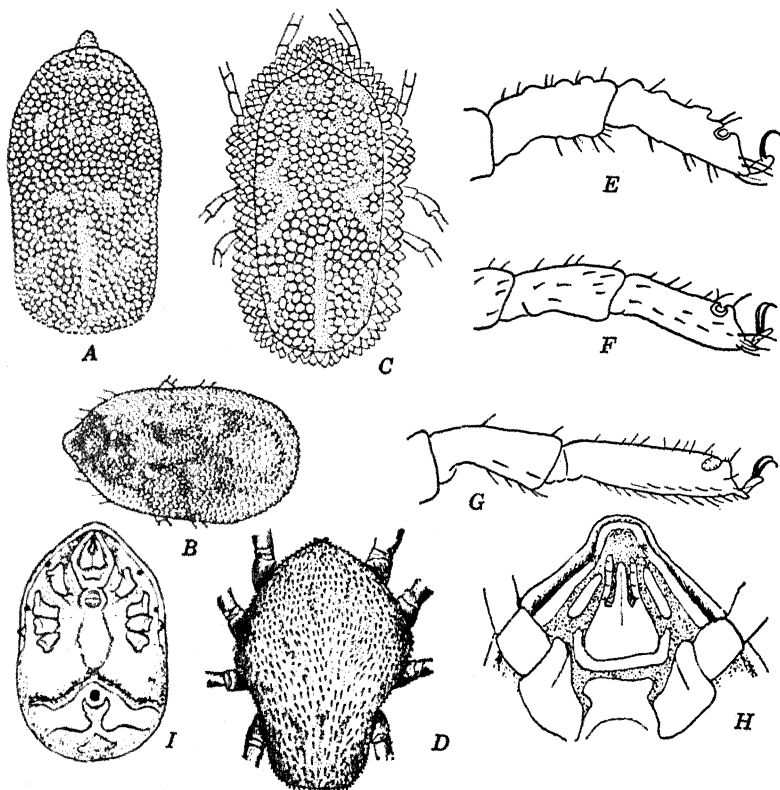


FIG. 171. Species and details of *Ornithodoros* and *Otobius*: A, *O. turicata*; B, *O. rudis*; C, *O. talaje*; D, *Otobius megnini*, nymph; E, F, and G, first leg of ♀ of *O. turicata*, *O. rudis*, and *O. talaje*, respectively; H, anterior end of *O. talaje*; I, ventral view of *O. coriaceus*. (B and C adapted from Brumpt, *Précis de parasitologie*, Masson, 1949. D, after Marx from Banks, *U.S. Bur. Ent. Tech. Bull.* 15. E, F, and G after Cooley and Kohls, *Am. Midland Naturalist Mon.* 1, 1944.)

- 3b. Tubercles small; a few small disc-like areas without tubercles (Fig. 171B); a distal hump on tarsus 1; Panama and northern South America; principal relapsing fever vector in those sections *rudis*.
 4a. No cheeks; hood of capitulum projects beyond anterior end of body (Fig. 171A) (*turicata* group) 5.

- 4b. Cheeks are rounded non-movable flaps at sides of camerostome; hypostome very small (145 μ long); tubercles very fine. High mountains west of Continental Divide, Arizona to Idaho, also in eastern Colorado; vector of relapsing fever *hermsi*.
- 5a. Tubercles in mid-dorsal region about 10 per linear mm.; hypostome over 600 μ long. Southwestern U. S. and Mexico north to Kansas, and Florida; vector of relapsing fever *turicata*.
- 5b. Tubercles in mid-dorsal region about 18 per linear mm.; hypostome 400 μ long or less; Wyoming and Washington; probably vector of relapsing fever *parkeri*.

Important Genera and Species of Ixodidae. Numerous species of the family Ixodidae occasionally attack man, but few habitually do so. Species belonging to a number of different genera are concerned with transmission of many important human and animal diseases and with the causation of tick paralysis. The important species involved in the various types of disease will be discussed under separate headings below.

Ixodes contains several important species. *I. ricinus*, the castor bean tick of Europe, transmits a piroplasmosis (*Babesia bovis*) of cattle in Europe and a virus disease of sheep, louping ill, in Great Britain. *I. persulcatus* is the principal transmitter of "spring-summer" encephalitis in Russia. *I. holocyclus* of Australia transmits a form of tick typhus in Queensland and also carries Q fever from bandicoots to cattle, making it accessible to man. Several species may cause tick paralysis (see p. 564). Several species occur in the United States, annoying dogs and occasionally man.

Amblyomma is a large genus of world-wide distribution. It is of great importance in the Americas in connection with the transmission of spotted fever and possibly other rickettsial diseases. *A. cajennense*, a common pest of domestic animals and man throughout tropical America, is the main transmitter of spotted fever in Brazil and Colombia. The lone-star tick, *A. americanum*, so called because of the single white spot on the scutum of the female (Fig. 176), is a transmitter of spotted fever in Texas and Oklahoma, where it is the commonest tick attacking man. It has also been found infected with Bullis fever. *A. maculatum*, the Gulf Coast tick, with fine silvery markings on the scutum, commonly attacks the ears of cattle as an adult; the immature stages have been found on meadow larks. Its bites often lead to screwworm infection; 50,000 cases were reported in 1935. This species has also been found to harbor a *Rickettsia* similar if not identical to that of boutonniere fever in Europe. The closely related tick-bite fever of South Africa may also be transmitted by an *Amblyomma*, *A. hebraeum*.

Hyalomma contains a number of important Old World species. Several, perhaps all, cause bad wounds when they feed on domestic

animals, and they are efficient transmitters of rickettsias causing human and animal diseases. In Africa secondary infection by screwworms frequently follows in the wound caused by *H. rufipes*. Several species harbor and transmit Q fever organisms in Africa. Various members of this genus are important vectors of *Theileria* infections (see p. 215) among cattle, sheep, camels, and horses in the Old World.

Haemaphysalis contains a rabbit tick, *H. leporis-palustris*, that transmits spotted fever and tularemia among reservoir hosts in America (see p. 574), and another, *H. humerosa*, that transmits Q fever among bandicoots in Australia. *H. leachi* is a transmitter of tick-bite fever of man, and also of piroplasmosis of dogs, in South Africa. *H. concinna* is reported as a vector of tick typhus in the Soviet Far East.

Rhipicephalus contains several important transmitters of piroplasmosis in the Old World, particularly *R. bursa* and *R. appendiculatus* among large domestic animals and *R. sanguineus* among dogs. The latter species, which has been imported and is now common in our southern states, is the principal carrier of boutonneuse fever in Europe and North Africa, but is only one of several important vectors in tropical Africa. It harbors a mild rickettsial disease in Texas and has been found naturally infected with spotted fever in Mexico. It is also the carrier of canine piroplasmosis (see p. 576).

Boophilus, unlike most of the previously mentioned genera, contains one-host ticks attacking cattle and other ruminants; they are the transmitters of *Babesia bigemina*, the cause of Texas or redwater fever, a piroplasmosis of cattle. *B. annulatus* has been almost exterminated in the United States, except in a few places in Florida and along the Rio Grande, where it survives on deer.

Dermacentor contains species of prime importance to man in the United States. *D. andersoni* and *D. variabilis* are important transmitters of spotted fever. *D. andersoni* has been referred to as a "veritable Pandora's box" of disease-producing agents, among which, besides spotted fever, are anaplasmosis, tularemia, brucellosis, *Salmonella enteritidis*, a bacterial "moose disease," Q fever, Colorado tick fever, and several forms of virus encephalomyelitis. Many of these can be transmitted by *D. variabilis* also, and both species can cause tick paralysis (see p. 564). *D. sylvarum* of Siberia transmits a rickettsial disease and a virus encephalitis, and *D. marginatus* of Europe and Siberia transmits piroplasmosis of dogs and horses.

The species are largely confined to North America, Europe, and Asia. They are ornamented with silvery markings, abdominal festoons, well-developed eyes, and oval or comma-shaped spiracular plates. Several species (*andersoni*, *variabilis*, *occidentalis*) in their larval and nymphal

stages attack rabbits and rodents, and in their adult stages attack rabbits and larger mammals, but *albipictus* is a one-host tick of large mammals. Following is a key to the North American adults according to Cooley (1938):

Key to Important Species of *Dermacentor* in North America

- 1a. Spurs on coxa I widely divergent (Fig. 172A); southwestern United States, mainly on rabbits; a possible transmitter of spotted fever among rabbits *parumapterus*.
- 1b. Spurs on coxa I with proximal edges parallel or a little divergent (Fig. 172B) 2.

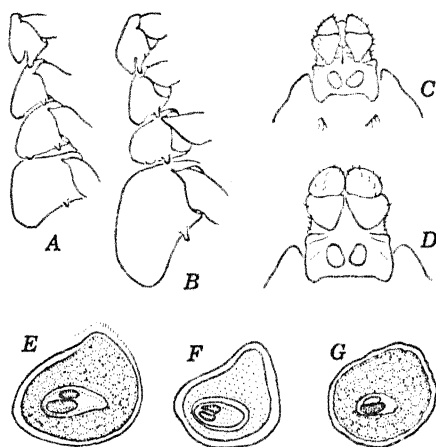


FIG. 172. Details of species of *Dermacentor* to illustrate key. A, coxa of *D. parumapterus*; B, same of *D. andersoni*; C, capitulum of *D. andersoni*; D, same of *D. occidentalis*; E, spiracular plate of *D. albipictus*; F, same of *D. variabilis*; G, same of *D. andersoni*. (Adapted from Cooley, N.I.H. Bull. 171.)

- 2a. Spiracular plate oval, without dorsal prolongation and with goblets (bead-like structures under spiracular plate) few and large (Fig. 172E); widely distributed in North America, a one-host tick, mainly on deer, etc.; probably not concerned with spotted fever, though an experimental vector *albipictus*.
- 2b. Spiracular plate oval, with dorsal prolongation (Fig. 172F, G), and with goblets many or of moderate numbers 3.
- 3a. Caudal projections from postero-lateral angles of dorsal side of basis capituli (cornua) long (Fig. 172C); west coast, southern Oregon; larvae on rodents, adults on horse, deer, sheep, cow, dog, and man; a known carrier of tularemia and a suspected one of spotted fever *occidentalis*.
- 3b. Cornua short or of moderate length (Fig. 172D) 4.
- 4a. Spiracular plate with goblets very numerous and small (Fig. 172F); eastern N. A., west to eastern Montana and central Texas, also western California; larvae on rodents, adults on many large animals but principally

- dogs; a transmitter of spotted fever and tularemia, experimental vector of anaplasmosis *variabilis*.
- 4b. Spiracular plate with goblets moderate in size and number (Fig. 172G); northwestern North America, south to northern New Mexico and Arizona, west to Sierras and Cascades, east to western Dakotas and western Nebraska, scattered records on west coast; larvae on small rodents, adults on all sorts of large mammals; vector of Rocky Mountain spotted fever and other diseases (see p. 569) *andersoni*.

Injury from Bites

The wounds made by ticks, especially if the capitulum is torn off in a forcible removal, are very likely to become infected and result in inflamed sores or extensive ulcers, not infrequently ending in blood poisoning. Some species seem more prone to do this than others. The writer was once nearly "done in" by the bite of a tick in California, probably *Dermacentor occidentalis*, which has a bad reputation.

Ticks may also be the cause of a serious or even fatal anemia when present in large numbers. Such anemias have been observed in horses, moose, sheep, and rabbits. Jellison and Kohls in 1938 found that 60 to 80 or more female *D. andersoni* feeding on rabbits would kill them in 5 to 7 days. According to Schuhardt in 1940, rats exposed to *Ornithodoros turicata* in his "ticktorium" die after 3 hours' exposure. Development of immunity to tick bites is discussed on p. 511.

Ticks can usually be removed successfully by gentle pulling, although sometimes the mouth parts of species of *Ixodes* and *Amblyomma*, which have long hypostomes with ugly barbs, may break off in the flesh. If the tick is jerked off, the whole capitulum may tear off. Most ticks will not let go even if touched by chemicals that kill them. Repellants and acaricides for ticks are discussed on p. 519. Application of a disinfectant should follow removal of ticks.

Tick Paralysis. More serious than the painful wounds made by ticks is a peculiar paralyzing effect of tick bites, known as tick paralysis. This effect is produced only by rapidly engorging female ticks, especially when attached on the back of the neck or at the base of the skull. In one case a male tick was suspected, but the evidence is not convincing. There is no evidence of any infective organism being involved. The cause of the paralysis is still obscure, but several investigators have obtained evidence that the eggs of ticks contain a highly toxic substance or that such a substance is formed during their development; it evidently makes its way to the salivary glands, since it is transmitted by the bites. Not all ticks produce the effect, but it is not limited to any one genus, nor does it extend to all the members of any one genus. In North America, *Dermacentor andersoni* and *D. variabilis* are responsible; in

Australia, *Ixodes holocyclus*; in Crete, *Ixodes ricinus* and *Haemaphysalis punctata* (suspected); in Somaliland *Rhipicephalus simus*, and in South Africa *Ixodes rubicundus*, *Hyalomma transiens*, and *R. simus*. In Russia *Ornithodoros lahorensis* causes paralysis, but only when present in large numbers. *Rhipicephalus sanguineus* in Yugoslavia was found to contain the toxin. In one case in British Columbia, *Haemaphysalis cinnabarina* was incriminated.

Since the paralysis is not invariably produced even by ticks situated at the base of the neck, it is possible that the bite must pierce or come in contact with a nerve or nerve ending. The paralysis usually begins in the legs and may result in complete loss of their use; it gradually ascends during the course of 2 or 3 days, affecting the arms and finally the thorax and throat. Unless the heart and respiration are affected, recovery follows in 1 to 6 or 8 days after removal of the engorging female ticks, even though other ticks remain. If the engorging ticks are not removed, the affection may result in death from failure of respiration or in spontaneous recovery after a few days or a week. The disease as observed in Australia differs from the North American type in that improvement is less immediate after removal of the offending tick. Paralysis of man and animals, particularly cattle, sheep, dogs, and cats, is frequent in northwestern United States and Canada. In South Africa sheep are paralyzed but human cases are doubtful. It is by no means certain that all cases reported in animals are true tick paralysis, since symptoms that might be confused may be caused by tick-borne infections—Babesiidae, Anaplasma, rickettsias, viruses, or bacteria. A "moose disease" in northern Minnesota and Ontario suspected of being tick paralysis was seemingly due to a paralysis-causing bacillus, *Klebsiella paralytica*, harbored by the tick, *Dermacentor albipictus* (see Wallace, Cahn, and Thomas, 1933). Most human cases are in children and are most frequent in girls, whose long hair conceals attached ticks. Some of the cases are fatal.

Ticks as Vectors of Disease

Ticks play an extremely important role as transmitters of disease to domestic animals and, fortunately to a somewhat less extent, to man. They are of outstanding importance in the transmission of organisms of six principal types: (1) spirochetes of relapsing fever, (2) rickettsias of spotted fever and related diseases of man and animals, (3) Babesiidae, causing many diseases of prime importance to domestic animals, (4) *Pasteurella tularensis*, the bacterium of tularemia, (5) *Anaplasma*, and (6) filtrable viruses of several types, including some causing encephalomyelitis. The special relation of ticks to the diseases caused

by these six types of disease agents is considered in separate sections below. *Rhipicephalus sanguineus* and probably others are intermediate hosts for *Hepatozoon canis* (see p. 219), causing infection when swallowed. *Dermacentor andersoni* and *Ornithodoros turicata* have been found to harbor and transmit a bacillus, *Salmonella enteritidis*, which causes a paratyphoid-like disease in rodents and sometimes gives trouble in experiments.

In addition to the species which serve as transmitters, others may function as conservators, harboring the disease agents for long periods of time, perhaps for life, without normally transmitting them. Certain species of *Ornithodoros*, for instance, are conservators of rickettsias, *Trypanosoma cruzi*, and *Pasteurella tularensis*.

TICKS AND RELAPSING FEVER

Many species of *Ornithodoros* transmit the spirochetes of relapsing fever to man and animals in various parts of the world, including tropical and north Africa, western Asia, Spain, Central and South America, and the western half of the United States and Canada, where outbreaks have been recorded from Texas to British Columbia and from Kansas to California. Not all species of *Ornithodoros* are capable of transmitting spirochetes, but in all the proved cases of transmission of mammalian relapsing fever by ticks, species of *Ornithodoros* have been involved, whereas species of *Argas* are the usual transmitters of relapsing fever of fowls.

The spirochetes in various parts of the world and in different hosts and vectors resemble each other very closely morphologically, but they differ in immunological reactions, pathogenicity for various animals, etc., but particularly in their peculiar vector specificity (see p. 52). Each species of tick transmits its own spirochete but fails to transmit spirochetes normally transmitted by other species. Closely related ticks such as *O. turicata* and *O. parkeri* in North America are distinguished with greater certainty by their ability to transmit particular strains of spirochetes than by their morphological characters. However, even strains of one species may differ in their ability to harbor particular strains of spirochetes. A discussion of relapsing fever and of the relation of the spirochetes to ticks can be found in Chapter 4, pp. 51-57.

Species Involved. *Ornithodoros moubata* of tropical Africa and Madagascar (Fig. 173) is the only species of its genus which has become an unconditional human parasite, normally residing in human habitations, although it often inhabits pigpens and warthog burrows. A related species, *O. savignyi*, widely distributed in Africa and western Asia to India and Ceylon, seems to be dallying with the idea of becoming

domestic, for in addition to frequenting cattle, pigpens, stables, etc., it sometimes overruns native bazaars, but it is never found inside of human habitations. It is only within the range of these two species that relapsing fever can be considered primarily a human disease and perhaps only in the range of *O. moubata*, for *O. savignyi*, although experimentally infectible, has not been found *naturally* infected.

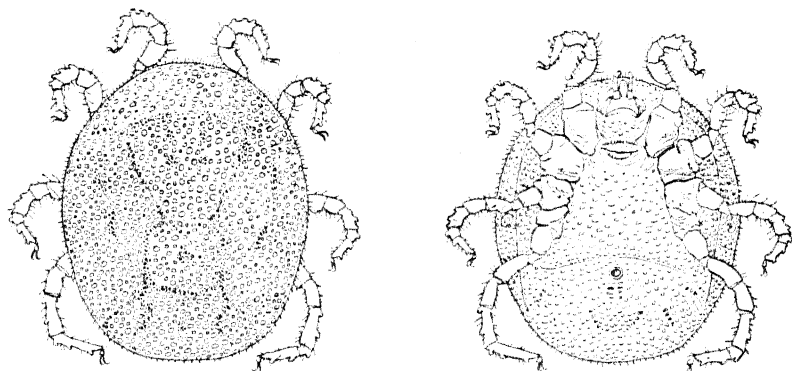


FIG. 173. *Ornithodoros moubata*, dorsal and ventral views. (From drawings supplied by Hoogstraal.)

O. rudis (Fig. 171B) readily enters human habitations with rats in Panama and northern South America and is undoubtedly responsible for most of the relapsing fever in that area. *O. talaje* (Fig. 171C), often confused with *O. rudis*, enjoys the blood of rats and pigs but shows a definite aversion to that of man, so if it enters houses it seldom makes its presence known. In California *O. hermsi* inhabits the nests of chipmunks. The chipmunks move into mountain cabins in the Sierras during the winter and share their spirochete-infested ticks with vacationers in the summer.

With the exception of these instances in which the ticks invade human residences and there transmit their spirochetes, human relapsing fever results from intrusion upon the natural habitats of the ticks—in pigpens, caves, burrows, etc. The important transmitters of sporadic human relapsing fever are briefly discussed on pp. 52–53. Apparently *O. coriaceus* of southern California and *O. lahorensis* of the Middle East and Central Asia are *not* transmitters. A key to the important American species of *Ornithodoros* is given on pp. 559–561.

HABITS. The habits and life cycles of the various species of *Ornithodoros* differ only in details. The ticks are oval or elongated, usually somewhat pointed anteriorly, and have the leathery, mud-colored body

covered with tubercles, ridges, or variously shaped protuberances. They do not thrive in places where moisture is excessive but can stand a surprising amount of desiccation, hence their frequency in dry, dusty regions.

In the case of *O. moubata* and *O. savignyi* the larvae molt and become nymphs a few hours after hatching, before partaking of their first meal. This is not true of the American species, however, which start looking for a place to drill almost at once. In some species, e.g., *talaje*, the larvae remain attached to a host for several days, but in others, e.g., *turicata*, they stay on only 10 minutes to a few hours; this is always true with the nymphs and adults, which can become distended like berries in this time. The nymphs feed and molt a number of times, and the adults feed repeatedly between the laying of batches of eggs. During and just after feeding some species exude fluid from a pair of coxal glands opening just behind the first coxae, enough to bathe the ventral surface of the tick. Relapsing fever spirochetes are transmitted either by the coxal fluid or directly by the bite.

O. moubata lives in floors, crevices, thatch, etc., of native huts and rest houses along routes of travel, after the manner of bedbugs, and is sometimes a great pest. It is dispersed in bedding carried by caravans. *O. savignyi*, as already noted, is not an indoor tick. *O. erraticus* commonly lives in rodent burrows, sometimes in pigpens or fox dens; in the burrows it feeds on anything from toads and lizards to burrowing owls and porcupines.

In the Americas the habits of *O. rudis* and *O. hermsi* have already been mentioned. *O. parkeri* is abundant in burrows of ground squirrels and prairie dogs. *O. turicata* is a very indiscriminate feeder, taking its blood where it finds it; in Mexico it attacks pigs, in Kansas it has been found in burrows of rodents and sand holes of terrapins, and in Texas it haunts caves where it promptly transmits relapsing fever to anyone venturing into them. Since these ticks can live at least 7 years with food and 5 years without it and can pass the spirochetes to their offspring generation after generation, it is little wonder that spirochete infections are common among tick-bitten animals.

Control. Control methods vary with the species of *Ornithodoros*. *O. moubata* must be controlled as are bedbugs—by cleanliness, elimination of hiding places, fumigation, or spraying with BHC. African huts remain free from this tick for a year after spraying with Lindane, at the rate of 200 mg. per sq. ft., and for over 2 years after 300 mg. per sq. ft. Dusting with 0.5 per cent BHC (3.2 lb. per 1000 sq. ft.) is also effective. *O. savignyi* usually conceals itself to a depth of an inch in dusty soil of camp sites, cattle stalls, etc., and can be reduced by har-

rowing the surface of the ground, strewing dry grass and brush over it, and burning it. Locally, dusting with BHC is effective. Control of *O. rudis* may involve rat elimination, whereas getting rid of *O. hermsi* demands inhospitality to chipmunks. The other species may need to be attacked in animal pens or shelters by the liberal use of turpentine, creosote, or BHC, but in their natural wild habitats they need only to be left alone.

TICKS AND SPOTTED FEVER AND OTHER RICKETTSIAL DISEASES

General Considerations. Tick-borne rickettsial diseases (see p. 528), or tick typhus, as Megaw calls them collectively, occur in many parts of both the Old and New World. A number of different strains, or species according to some, are recognized by their immunological reactions and sometimes by their pathogenicity. Unlike the rickettsias of true typhus, the tick-borne varieties invade the nuclei as well as cytoplasm of the cells and so are placed in a separate subgenus, *Dermacentroxenus*.

In the ticks the organisms invade the entire body and are transovarially transmitted. It is open to question whether a vertebrate reservoir host is actually needed, but epidemiological evidence suggests that it is. Jellison in 1946 pointed out that the distribution of spotted fever in northwestern United States corresponds remarkably closely with the distribution of one species of cottontail rabbit, *Sylvilagus nuttalli*. The distribution of *Dermacentor andersoni*, the only transmitter to man in the Northwest, also coincides with that of this rabbit; some other species of *Dermacentor* in North America, e.g., *D. variabilis* and *D. occidentalis*, have distributions corresponding with those of particular species of cottontails. Jellison further pointed out that cottontails also occur in parts of Mexico, Colombia, and Brazil where spotted fever is endemic. Since cottontails are the only animals that *Dermacentor andersoni* favors as a host in all its stages, suspicion attaches to them as reservoir hosts of spotted fever. Yet it is a curious fact that, in spite of the readiness with which spotted fever can be inoculated into rodents, the rickettsia has not yet been isolated from any wild rodent.

In the Old World dogs have been found to serve as reservoirs for *Rickettsia conorii* of boutonneuse fever, and it is possible that they may be reservoir hosts for spotted fever also. Ground squirrels, marmots, and gerbils are also susceptible to *R. conorii*.

Types of Tick-Borne Rickettsial Diseases. The principal forms of tick-borne rickettsial disease are: (1) spotted fever in North and South America, caused by *R. rickettsii*; (2) boutonneuse fever around the Mediterranean and the same or a very closely related disease known

as tick typhus or tick-bite fever in tropical and South Africa, central Asia, eastern Siberia, Pakistan, India, and Malaya, caused by *R. conorii*; (3) North Queensland tick typhus, caused by *R. australis*; and (4) some animal diseases caused by rickettsia-like organisms of the genus *Ehrlichia*, including *E. canis* of dogs, *E. bovis* of cattle, and *E. suis* of pigs (see p. 228).

All the human diseases, belonging to the first three groups, are characterized by a severe rash or blotching of the skin, including face, palms, and soles; headache; body pains; fever; and a positive Weil-Felix reaction, i.e., agglutination of OX19 or OX2 strains of *Proteus* by the serum of infected persons or animals. In the Old World forms there is usually a button-like black ulcer (eschar) at the site of the infective bite, hence the name boutonneuse, French for button-like.

In addition to typhus-like tick-borne diseases there are two rickettsial infections of somewhat different nature that are transmitted by ticks—Bullis fever in Texas, and Q fever, which is probably cosmopolitan.

Spotted Fever and Its Vectors. This disease has long been known as a common and dangerous infection in the Rocky Mountain region of northwestern United States and Canada, especially Montana and Idaho. Since 1930 sporadic cases have become increasingly frequent in other parts of the United States, particularly on the middle Atlantic coast. The same disease, immunologically indistinguishable, occurs in parts of northern Mexico (where it is called "pinto fever"), in parts of Colombia, and in the São Paulo region of Brazil.

The disease is transmitted by the bites of ticks, but it takes about 2 hours of attachment before transmission is successful. The only tick known to be involved in transmission to man in the northwest is *Dermacentor andersoni*. In the eastern and southern states it is mainly *D. variabilis*, although both *Haemaphysalis leporis-palustris* (see next paragraph) and *Ixodes dentatus* have been found naturally infected; in Texas and Oklahoma, *Amblyomma americanum*; in South America, *A. cajennense* and *A. striatum*. In Mexico the usual transmitter is not known with certainty, but strains of *R. rickettsii* have been isolated from *Rhipicephalus sanguineus* both in Texas and Mexico, and the Mexican *Ornithodoros nicollei* is a capable vector experimentally. In the northwest *O. parkeri* is an experimental vector, and a few cases of the disease have been found within the domain of *Dermacentor occidentalis* on the west coast.

The rabbit tick, *Haemaphysalis leporis-palustris*, although it never bites man, is a factor in keeping the disease alive among its reservoir hosts. The virus carried by the rabbit tick, as recovered in nature, is

very mild in form as compared with the virulent strains obtained from *D. andersoni* and *D. variabilis*; when these species become numerous in a locality and begin transmitting the disease to other kinds of rodents and to man, virulent strains appear. It is not known whether the stepping-up of virulence is due to passage of the *Rickettsia* through other animals than rabbits or to development in *Dermacentor* instead of *Haemaphysalis*. Another species which may be an important transmitter among rabbits is *D. parumapterus*.

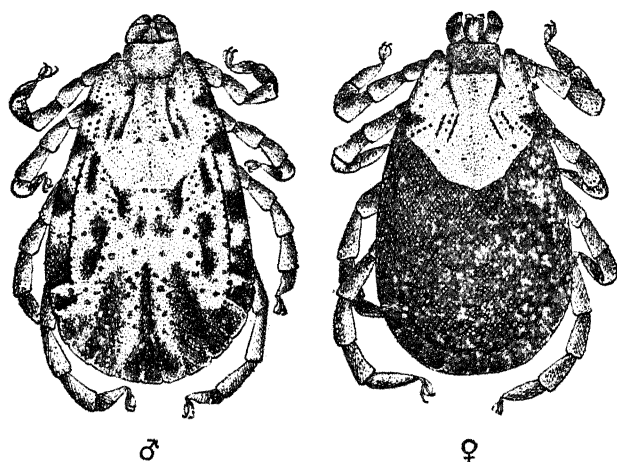


FIG. 174. Spotted fever tick, *Dermacentor andersoni*, ♂ and ♀, $\times 12$.

***Dermacentor andersoni* and Other Species of *Dermacentor*.**

D. andersoni (Fig. 174) is pre-eminent as a transmitter of spotted fever because during its immature stages it is a parasite of rodents, but as an adult it attacks a great variety of larger animals, willingly including man. It is a handsome reddish-brown tick, with the large dorsal shield of the male and the smaller one of the female conspicuously marked with silver. The six-legged larvae (Fig. 175B), of which there are about 5000 in a brood, attach themselves to rabbits or rodents, especially squirrels of various kinds. Usually the larvae, and the nymphs also, attach themselves about the head and ears of their host. After a few days the larvae drop, transform into nymphs (Fig. 175), and again attack their rodent or rabbit hosts.

After dropping off these and transforming into adults they no longer pay attention to the smaller rodents but seek larger animals, especially preferring horses and cattle, though they readily attack other wild and domestic animals and man. Unlike most ticks, this species may take

2 or even 2½ years to complete its life cycle. The winter is passed in either the nymphal or adult stage.

D. variabilis and *D. occidentalis* have similar life cycles. *D. variabilis* seems to have a strong preference for meadow mice and white-

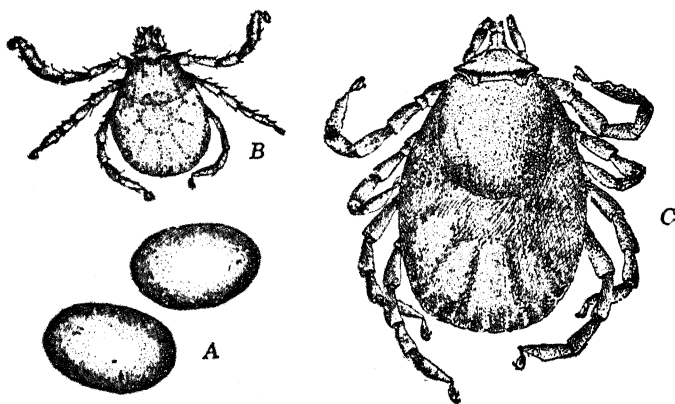


FIG. 175. Development of spotted fever tick, *Dermacentor andersoni*; A, eggs; B, larva; C, nymph. $\times 30$.

footed mice in its immature stages and for dogs in the adult stage, but *D. occidentalis* has the same wide range of hosts as *D. andersoni* in both

immature and adult stages. A key for the differentiation of the important North American species of *Dermacentor*, with geographic distributions, is given on pp. 563–564.

***Amblyomma americanum* and *A. cajennense*.** *A. americanum*, the lone-star tick (Fig. 176), has a wide distribution in south central United States and is the commonest tick attacking man in Texas and Oklahoma; it is also abundant on deer, sheep, cattle, dogs, and rodents. According to Parker, Kohls, and Steinhaus (1943) the fact that this tick bites man in all its stages

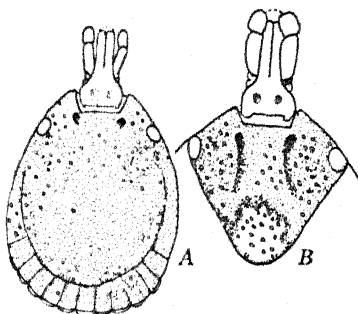


FIG. 176. *Amblyomma americanum*, lone-star tick. A, male; B, dorsal shield and capitulum of female. (Adapted from Cooley and Kohls, *J. Parasitol.*, 30, 1944.)

and that its nymphs sometimes occur in immense concentrations within small areas may account for the multiple family infections occurring where it is the suspected transmitter.

A. cajennense is a common and widespread tick from the southernmost tips of the United States to Argentina. It can transmit spotted fever experimentally, and the epidemiology suggests it as the principal transmitter in Brazil and Colombia. Its preferred adult host seems to be the horse, but men and dogs are readily attacked.

Boutonneuse Fever and "Tick Typhus." As noted on pp. 569-570, tick-borne typhus-like diseases occur in many parts of southern Europe, Asia, and Africa, all being very closely related to boutonneuse fever of the Mediterranean region, if not identical with it. These diseases are all transmitted readily by *Rhipicephalus sanguineus* and certain other ticks, but are not readily transmitted experimentally by *Dermacentor andersoni*. Since *D. nuttalli* and *D. sylviarum* are the transmitters of "tick typhus" in central Asia and Siberia, with marmots and *Microtus* suspected as reservoirs, this form of the disease may be closer to spotted fever than are the others. In eastern Siberia *Haemaphysalis concinna* is also said to harbor the rickettsia of "tick typhus." In Africa south of the Sahara there are potential transmitters in practically all ecological situations. Of these, *R. sanguineus* is primarily a dog tick; except in the Mediterranean region it rarely bites man. *Haemaphysalis leachi* is also primarily a dog tick, but in its immature stages attacks rodents. *R. simus* and *R. appendiculatus* attack a wide variety of wild and domestic animals. *Amblyomma hebraeum* is a vector in its immature stages, but feeds principally on cattle as adults; it is also an important vector of "heartwater" fever of ruminants (see p. 230). Hoogstraal suspects *Hyalomma rufipes* as a vector in drier areas where cattle are maintained.

Many rodents and also dogs serve as reservoir hosts for *Rickettsia conorii* of boutonneuse fever, but dogs show no evidence of infection except a positive Weil-Felix reaction.

Tick typhus of North Queensland, caused by *Rickettsia australis*, is transmitted by *Ixodes holocyclus*. *Rickettsia* (*Ehrlichia*) *canis* of dogs, very common in some parts of Africa and Asia, is transmitted by *Rhipicephalus sanguineus*.

Rickettsial disease agents have been isolated by Anigstein and Bader from *Amblyomma americanum* and *A. maculatum* collected from cattle; those from *americanum* are virulent, those from *maculatum* mild. The latter were previously isolated by Parker et al. in Texas in 1939, and were recently reported in Mississippi by J. S. White. The disease produced by this organism is called "maculatum fever." The interrelations of these various rickettsial infections are still very obscure, and much is still to be learned about the extent to which they are modified by passage through different vectors or development in relatively insusceptible hosts such as dogs, pigs, and cattle.

Q Fever. This rickettsial disease, caused by *Coxiella burnetii*, was first discovered in 1937 in Australia where it is transmitted among bandicoots by *Haemaphysalis humerosa* and from these animals to cattle and possibly occasionally to man by *Ixodes holocyclus*. A year later this infection was discovered in *Dermacentor andersoni* in Montana. Subsequently it has been found to be widely distributed, probably cosmopolitan, having been found in various parts of the United States, Panama, Switzerland, all around the Mediterranean, and in many parts of Africa. In some areas it is a very common though frequently overlooked disease of man and domestic animals. Many ticks, including both Ixodidae and Argasidae, have been found naturally infected. Experimentally, transovarial transmission has been reported for *Ornithodoros moubata*.

Unlike the typhus-like diseases, Q fever is not primarily dependent upon ticks for transmission to man; in fact, very few human cases have resulted from tick bites. Human outbreaks usually occur among stock handlers and people working in slaughterhouses and dairies. It spreads with remarkable facility among laboratory workers, apparently being acquired from dust; an outbreak was reported in laundry workers who handled soiled laundry from a laboratory doing work with Q fever. Infection also results from handling carcasses, drinking raw milk, and breathing dust around cattle pens, but there is no evidence of direct transmission from person to person.

Q fever is an influenza-like disease without a rash, causing fever, chest pains, and cough; in Europe it was called Balkan grippé or atypical pneumonia. Cattle and horses acquire light or inapparent infections, as do dogs and cats, but sheep and goats develop respiratory symptoms similar to those in man. In Greece natural infection in the latter animals was demonstrated by inoculation of milk into guinea pigs.

Bullis Fever. A previously unknown rickettsial disease first appeared in a few cases at Camp Bullis, Texas, in 1941 and seems now to be permanently established in central Texas. Rickettsias were isolated from cases and also from a naturally infected *Amblyomma americanum* by Anigstein and Bader. The *Rickettsia* involved is said not to be related to that of either Q fever or spotted fever. There are very few small rodents in the Bullis fever area; the principal hosts of *A. americanum* are deer, sheep, and goats.

TULAREMIA AND OTHER BACTERIAL DISEASES

Tularemia or rabbit fever is another disease of rabbits and rodents transmissible to man; human cases have been reported throughout the United States, Canada, and Alaska, and from Scandinavia to Japan

in the Old World. The disease is characterized by a local ulcer at the site of inoculation, with enlarged and painful lymph glands in the vicinity and such generalized symptoms as fever, prostration, general aches, and localized pains. The fever lasts for several weeks, usually with an intermission between the third and sixth days. The disease rarely is fatal, but localized pains, weakness, and lassitude may last for several months, and a lasting immunity develops. Diagnosis is made by inoculating material from the ulcer or inflamed glands into laboratory animals or by an agglutination test. Streptomycin is useful in treatment.

The disease is caused by a bacillus, *Pasteurella tularensis* (see p. 235), closely related to the plague bacillus. It infects many mammals and even some birds, but rabbits and ground squirrels seem to be preferred. Severe outbreaks have been reported among sheep, jack-rabbits and beavers. In Arkansas hunting dogs are commonly infected, and infected ticks (*Amblyomma americanum*) are found on them.

Experimentally the disease can be transmitted by many different arthropods, including lice, fleas, deerflies, and ticks, but the last are probably the primary transmitters among natural hosts. It is transovarially transmitted by *Dermacentor andersoni*, *D. variabilis*, and *Haemaphysalis leporis-palustris*, which are the commonest transmitters to rabbits in this country. The ticks transmit the disease either by their bites or by fecal contamination of skin abrasions; mere handling of an infected tick and subsequent rubbing of the eye may cause infection. The disease is also transmitted by contact and is frequently acquired by handling diseased animals, especially rabbits. In an epizootic among beavers and muskrats in Montana and Wyoming, there were thirty-eight known human cases from handling these animals. A remarkable feature, still not adequately explained, was the pollution of all the water and mud in rivers and tributaries over a large area for a period of 16 months. In spite of this, human infections from drinking the water or swimming in it are few. In 1934 a water-borne epidemic was reported in Turkey.

Another bacterial disease that Tovar in 1947 found ticks able to transmit is undulant fever or brucellosis. Naturally infected ticks (*Amblyomma cajennense* and *Boöphilus*) are found on infected animals and may play an important role in the spread of the disease among animals and to man. Hitherto this disease was known to be transmitted by contaminated food or water or with the milk or meat of infected animals.

Ticks do not transmit other bacterial diseases to man, but some species transmit *Salmonella enteritidis* to laboratory animals (see

p. 234), and *D. albipictus* has been found to harbor *Klebsiella paralytica*, associated with a "moose disease" (see p. 234). However, Anigstein and his colleagues have shown that ticks contain a substance that inhibits the growth of many kinds of bacteria.

PIROPLASMOSIS, ANAPLASMOSIS, AND VIRUS DISEASES

The small blood protozoans belonging to the family Babesiidae (see p. 213) are the cause of numerous important diseases in domestic animals. To these the name "piroplasmosis" is generally applied, since the organisms were once named *Piroplasma*. Man is peculiarly exempt.

Texas Fever and Other Piroplasmoses. Texas fever or "redwater fever" (briefly described on p. 215) is of enormous economic importance in cattle-raising countries. It was formerly prevalent in southern United States but has now been wiped out. Smith and Kilbourne in 1893 set a milepost in history when they discovered its transmission by cattle ticks, *Boophilus annulatus*. This is a one-host species, so it is obvious that a tick becoming infected on one animal would have no opportunity to infect another. It could not do so even if transplanted from one animal to another, for the organisms (*Babesia bigemina*) invade the eggs of the tick, and cyclical development takes place in the embryonic tissues of the developing offsprings (see p. 215). Many other species of *Babesia* are known to infect ruminants, horses, pigs, dogs, and even poultry. The life cycles of the various species are probably similar, since all of them are hereditarily transmitted in their tick vectors.

All the species of *Boophilus* seem to be able to serve as intermediate hosts for the *Babesia* of cattle, sheep, etc. In Europe *Ixodes ricinus* is an important transmitter of *B. bovis*, and species of *Hyalomma* and *Rhipicephalus* have been implicated in North Africa and elsewhere. *B. canis*, causing piroplasmosis in dogs, is transmitted by *R. sanguineus* in the tropics, by *Dermacentor marginatus* (= *reticulatus*) in Europe (this species also transmits a *Babesia* of horses), and by *Haemaphysalis leachi* in South Africa. According to Shortt, *B. canis* can be transmitted by subsequent stages of an infected tick as well as by its offspring. A related parasite of horses, *Nuttallia equi* (see p. 215), is transmitted by *Dermacentor nuttalli* and also by a one-host tick, *Hyalomma scutense*, in Russia.

The Protozoa of the related genus *Theileria* (see p. 215), one of which causes the deadly East Coast fever of cattle in Africa, differ in their life cycles (worked out for *T. dispar* by Sargent et al., 1936) since they are transmitted only by two-host or three-host ticks and never transovarially. Species of *Rhipicephalus* and *Hyalomma savignyi* are

the principal transmitters of East Coast fever, whereas various species of *Hyalomma* (*detritum*, *excavatum*, *savignyi*, and *punctata*) and *Boöphilus annulatus* are reported as vectors of a milder *Theileria* infection in North Africa and Turkey.

Aegyptianella pullorum, a protozoan inhabiting the blood corpuscles of chickens, ducks, and geese and believed to belong to the Babesiidae, occurs in southern Europe and Africa and is transmitted by *Argas persicus*. A similar organism has been reported from fowls in New York and Philadelphia.

Anaplasmosis. This frequently fatal disease, which causes fever, jaundice, and a very severe destruction of blood corpuscles in cattle and other animals, is characterized by dot-like bodies in the blood corpuscles, called *Anaplasma* (see p. 230). The disease is very commonly associated with *Babesia* or *Theileria* infections, since the tick vectors often have double infections. It can be transmitted by at least seventeen species of ticks belonging to several different genera and also by the intermittent feeding of biting flies. It can also be transmitted by ticks to their offspring.

Virus Diseases. Ticks have been shown to harbor and in some cases to transmit a number of viruses infective for man and animals. *Dermacentor andersoni* can transmit the western form of equine encephalomyelitis, and *D. variabilis* has been shown to do the same for the St. Louis strain. "Spring-summer encephalitis," occurring in forested areas of Siberia and the Russian Far East, is transmitted principally by *Ixodes persulcatus*, in which the virus is transovarially transmitted. This virus has been found in the central nervous system of rabbits and hares, and the presence of antibodies against it indicates that inapparent infections are very common both in man and in animals. Birds, also, are carriers. *I. persulcatus* is also reported to be a vector of Japanese B virus. In Colorado and neighboring states a febrile disease called Colorado tick fever, caused by a filtrable virus, is carried and transovarially transmitted by *Dermacentor andersoni*. The same or a closely related virus has been isolated from *D. variabilis* on Long Island. The disease is strikingly like dengue (see p. 727) in most respects, including a very marked leucopenia.

In northern England and Scotland louping ill, a virus disease attacking the central nervous system, is transmitted among sheep by ticks, principally *Ixodes ricinus*. It has been reported from Russia also. In experimentally infected *Rhipicephalus appendiculatus* the virus was not transovarially transmitted. Man is believed to be susceptible. In Kenya a virus disease with symptoms suggestive of yellow fever, called Rift Valley fever, which is very fatal for sheep, less so for cattle, and

mild for man, and which is usually transmitted by mosquitoes, has been found to survive in *Rhipicephalus appendiculatus* for a week after feeding on infected sheep.

Control of Ticks

Ticks on domestic animals were formerly controlled by sodium arsenite dips (about 0.16 per cent), which are still used to some extent, and by pasture rotation. By these methods and by federal quarantine the one-host cattle tick, *Boophilus annulatus*, and with it Texas or redwater fever of cattle, was eliminated from the United States, although a few of these ticks persist on deer in a few places in Florida, and sometimes cross the Rio Grande from Mexico on cattle or deer.

BHC, Chlordane, Toxaphene, and DDT (see p. 514) are most often used now, either as sprays at 0.5 to 0.6 per cent (or 0.03 per cent Lindane) or as dips at about 0.05 per cent. DDT is effective against *Boophilus* but much less against *Amblyomma* or *Rhipicephalus*, whereas for Toxaphene the opposite is said to be true. DDT, Chlordane, and Toxaphene prevent reinfection for about 2 weeks, BHC for much less time. Methoxychlor is best for dairy cows (see p. 613). Unfortunately strains of ticks resistant to BHC have developed in several parts of the world, and there are also arsenic-resistant strains. Pine tar oil, BHC emulsions, or 8 per cent DDT in grease, with 25 per cent sulfur added, are recommended for treatment of *Otobius* and *Amblyomma maculatum* in ears of animals.

Dogs can be freed of ticks by immersion or washing with 0.2 per cent piperonyl butoxide plus 0.01 per cent pyrethrins, 0.6 per cent BHC or 1 or 2 per cent DDT suspensions, or dust containing 0.6 per cent piperonyl cyclonone plus 0.05 per cent pyrethrins worked into the fur. Powders containing 10 per cent DDT or BHC are also useful.

Fairly good control of ticks on grassland pastures, effective for 5 or 6 weeks, can be obtained by spraying with DDT or Dieldrin from planes or helicopters at a dosage of 0.5 to 1 lb. per acre in a gallon of oil solution or in 15 gallons of emulsion. Hunter et al. in 1954 reported about 98 per cent control of *Amblyomma americanum* with 0.5 lb. per acre of Dieldrin as a dust. DDT or BHC dusts also give good control. BHC dusts or sprays are effective against *Argas persicus* in chicken houses. As repellents for man, *n*-butyl acetanilide is very effective against *Amblyomma americanum* but much less so against *Dermacentor*. Dibutyl adipate, hexylmandalate, and others are also good repellents (see p. 519).

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Bedbugs and Other Hemiptera

The Order Hemiptera. The order Hemiptera, comprising the true bugs, contains numerous species most of which are predaceous or feed on plant juices, but some of which habitually or occasionally suck blood. The most important of these are the bedbugs, which probably first became acquainted with man when he shared caves with bats and swallows during the Ice Age, and which have since become fully domestic, to the disgust of good housekeepers all over the world. Also important are the conenoses (*Triatominae*); these are large, fierce bloodsuckers, some species of which have become habitual residents in human habitations and in tropical America are the transmitters of Chagas' disease. In addition, not only the wild bloodsuckers but also many forms which are predaceous on insects may inflict painful and even dangerous bites.

The Hemiptera have an incomplete metamorphosis, the adult condition being attained gradually by successive molts of the nymphs (see p. 508). The mouth parts (Fig. 179, *left*) are fitted for piercing and sucking. There is a short labrum covering the bases of the mouth parts. The labium is in the form of a three- or four-jointed beak bent back under the head and thorax and grooved on the dorsal surface (ventral when bent under the head) to contain the stylet-like mandibles and maxillae. The maxillae are coarser and fit together to form two grooves—a large food channel and a small salivary duct. The hypopharynx and palpi are absent.

The wings, except in those forms, like the bedbugs, in which they are vestigial, are very characteristic; the first pair, called hemelytra, have the basal portion thickened and leathery while the terminal portion, which is sharply demarcated, is membranous (Fig. 177). The second pair of wings are membranous and fold under the others when

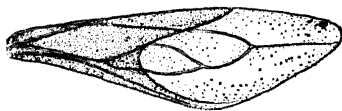


FIG. 177. A hemipteran wing (reduviid).

at rest. Many bugs have "stink glands" between the bases of the hind legs which secrete a clear volatile fluid by means of which they emit a strong offensive odor.

BEDBUGS (*CIMEX*)

General Account. The bedbugs belong to the family Cimicidae. They have broad, flat, reddish-brown bodies and are devoid of wings, except for a pair of bristly pads which represent the first pair of wings

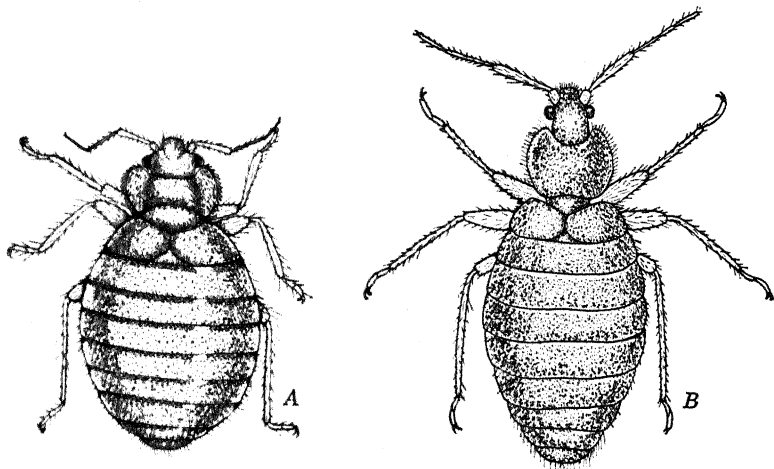


FIG. 178. Bedbugs. *A*, common bedbug, *Cimex lectularius*; *B*, Oriental or Indian bedbug, *C. hemipterus*. $\times 8$. (Adapted from Castellani and Chalmers, *A Manual of Tropical Medicine*, 1920.)

(Fig. 178). The eyes project prominently at the sides of the head, the antennae are four-jointed, and the beak is three-jointed (Fig. 179). The legs have the usual segments, the tarsi being three-jointed. The prothorax is large, indented in front for the head, and has flat lateral expansions. The mesonotum is small and triangular, bearing the wing pads, which nearly cover the metanotum. The abdomen is flat, its contour an almost perfect circle in unfed bugs, but elongated in full ones; it has eight visible segments, the first two (of nine) being fused. In males the abdomen is pointed at the tip, whereas in females it is evenly rounded. The greater part of the body is covered with bristles set in little cup-shaped depressions. These depressions are perforated at the bottom to allow for the passage of muscles which move the bristles. Murray describes having seen bugs raise the bristles upon meeting each other as cats raise their hairs or birds their feathers.

Bedbugs have a peculiar pungent odor known to all who have had

to contend with these pests; the adults have the stink glands situated in the last segment of the thorax, opening through a pair of ducts between the coxae of the hind legs. In the first four nymphal stages these glands are not present but are preceded by glands situated on the dorsal side of three of the anterior abdominal segments. The nasty odor of bedbugs has evidently inspired some faith in their medicinal value. Seven bugs ground up in water was said by Pliny to arouse

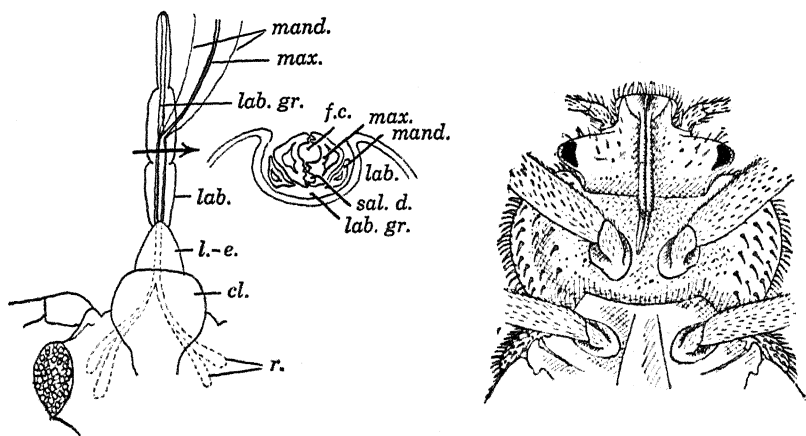


FIG. 179. Left, mouth parts of bedbug, with cross-section; *cl.*, clypeus; *f.c.*, food channel; *lab.*, labium; *lab.gr.*, labial groove; *l.-e.*, labrum-epipharynx; *mand.*, mandibles; *max.*, maxillae; *r.*, roots of mandibles and maxillae; *sal.d.*, salivary duct. (After Matheson, *Medical Entomology*, Comstock, 1950.)

one from a fainting spell, and one a day would render hens immune to snake bites. Even at the present time there are places in civilized countries where bedbugs are given as an antidote for fever and ague.

Species. The true bedbugs belong to the genus *Cimex*, but not all the species are human parasites; some confine their attentions, ordinarily at least, to birds and others, to bats. There are two widely distributed species that attack man; one is the common bedbug, *C. lectularius*, found in all temperate climates and sometimes also in tropical ones; the other is the tropical or Indian bedbug, *C. hemipterus* (formerly *rotundatus*), which is the prevalent species in the tropical parts of the world. It is distinguished by having less marked lateral expansions of the prothorax (Fig. 178). In west Africa another species, *Leptocimex boueti*, attacks man; it is a silky-haired, long-legged bug with small rectangular thorax.

Some other Cimicidae may become nuisances under special conditions. The proverbially superclean housekeepers of Holland villages,

for instance, are sometimes greatly chagrined to find bugs in their spotless houses, the bugs being *C. columbarius* derived from pigeons nesting in the roofs. Similar temporary invasions by *C. pilosellus* of bats sometimes occur in dwelling houses, especially when the bats are driven away or migrate. The silky-haired bugs of the closely related genus *Oeciacus*, which live in swallows' nests, also occasionally invade houses and cause much annoyance to the inhabitants, but the invasions are temporary; Myers in 1928 showed that this species requires bird blood before it will reproduce. The Mexican poultry bug, *Haematosiphon inodora*, is a related species resembling a bedbug but having longer legs, no odor, and a very long beak that reaches to the hind coxae. It is often a serious poultry pest in the dry parts of the southwest and sometimes invades houses and torments man. The Mexicans sometimes abandon or burn their huts to escape from them.

The interhostal traffic in bedbugs is not by any means a one-way affair, for the nests of sparrows and starlings, the burrows of rats, the attic roosts of bats, and also chicken houses and pigeon cotes are often invaded by hungry bugs that have been abandoned by their human sources of blood. The sparrows and starlings may frequently be a means of starting new colonies in other houses, but bats, contrary to popular opinion, probably rarely do, since they are not much given to visiting. Bugs found under bark and moss out of doors are not bedbugs but immature stages of other bugs that superficially resemble them.

Following is a key for the differentiation of the commoner Cimicidae likely to invade houses in America:

- 1a. Beak short, not extending behind first coxae (Fig. 179) 2.
- 1b. Beak long, extending to hind coxae; legs long; no odor; on poultry in southwestern United States *Haematosiphon inodora*.
- 2a. Body hairs short, set in sockets only on dorsal side; pronotum deeply concave in front; third and fourth joints of antennae markedly slender (*Cimex*) 3.
- 2b. Body hairs long and silky, set in sockets on ventral side also; pronotum not deeply concave; terminal joints of antennae only slightly more slender than basal joints; in nests of swallows; L. 4 mm. *Oeciacus vicarius*.
- 3a. Second and third joints of antennae about equal, third longer than fourth; L. 4 mm.; on bats *Cimex pilosellus*.
- 3b. Second joint of antennae shorter than third 4.
- 4a. Lateral parts of pronotum with flat lateral expansions (Fig. 178A); in human houses in temperate climates; L. 5 to 6 mm. *C. lectularius*.
- 4b. Similar but smaller, rounder; shorter and coarser antennae; prothorax less concave in front; in pigeon houses (doubtful if a distinct species) *C. columbarius*.
- 4c. Pronotum rounded to margin on dorsal side (Fig. 178B); in human houses in tropics; L. 5 to 6 mm. *C. hemipterus*.

Habits. Bedbugs are normally night prowlers and exhibit a considerable degree of cleverness in hiding away in cracks and crevices during the daytime. When hungry they will frequently come forth in a lighted room at night and may even feed in broad daylight. Favorite hiding places are in old-fashioned wooden bedsteads, in crevices between boards, under wallpaper, etc., into which they can squeeze their flat bodies. They sometimes go considerable distances to hide in the daytime and show remarkable resourcefulness in reaching sleepers at night. In the tropics newcomers often wonder why their heads itch under their sun helmets until they discover a thriving colony of bugs in the ventilator at the top.

When a bug is about to drill for blood the beak is bent forward and the piercing organs sunk into the flesh. Bugs seldom cling to the skin while sucking, preferring to remain on sheets or clothing. Since a fresh meal apparently acts as a stimulus for emptying the contents of the rectum, the adherence to the clothing is a fortunate circumstance, inasmuch as it precludes to some extent the danger of bedbugs infecting their wounds with excrement, as do ticks.

In the course of 10 or 15 minutes a full meal is obtained and the distended bug retreats to its hiding place. According to Cragg, *Cimex hemipterus* does not entirely assimilate a full meal for at least a week, although the bug is ready to feed again in a day or two, thus having parts of several meals in the stomach at once. Most bloodsucking insects completely digest one meal before another is sought.

Bedbugs are able to endure long fasts; they have been kept alive without any food whatever for over a year. Sometimes, however, bugs migrate from an empty house in search of an inhabited area. In cold weather they hibernate in a semitorpid condition and do not feed, but in warm climates they are active the year around. *C. lectularius*, according to Marlatt, succumbs at temperatures above 96° to 100°F. if the humidity is high. According to Bacot, unfed newly hatched bugs are able to withstand cold between 28° and 32°F. for as long as 18 days, though they are destroyed by exposure to damp cold after a full meal.

Hosts. Although man is undoubtedly the normal and preferred source of blood for *Cimex lectularius* and *C. hemipterus*, the bugs manage to get along surprisingly well on other kinds of blood. Johnson in 1937 found experimentally that bedbugs thrive even better on mice than on men and about equally well on chickens. They sometimes multiply in great numbers in chicken houses, dovecotes, and white-rat cages. Dogs and cats are frequently bitten also.

Life History. The eggs of bedbugs (Fig. 180A) are pearly white oval objects, furnished at one end with a little cap which is bent to one

side. The eggs are relatively large, about 1 mm. in length, and are therefore laid singly or in small batches, averaging about two a day. The total number of eggs laid is about 100 to 250. The bugs frequently return to the same places to oviposit until sometimes as many as 40 eggs have been accumulated.

The eggs hatch in 6 to 10 days during warm weather but are retarded in their development by cold. A week of freezing temperature reduces the hatching to 25 per cent. The freshly hatched bugs (Fig. 180B) are very small, delicate, and pale in color. The skin is normally molted five times at intervals of about 8 days before the final adult stage is

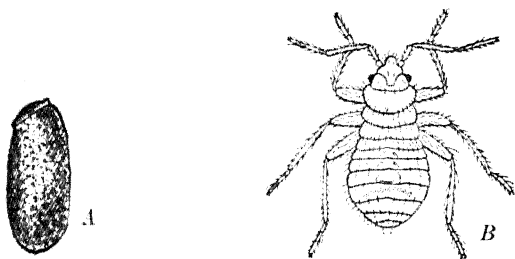


FIG. 180. Egg (A) and newly hatched larva (B) of bedbug. $\times 20$. (After Marlatt, *Farmer's Bull.*, 754, 1925.)

reached, at least one gluttonous feed being necessary before each molt in order to insure normal development and reproduction. However, the bug may gorge itself several times between molts. The several nymphal stages of the insect resemble each other quite closely except in the constantly increasing size and deepening color. The wing pads appear only after the last molt. The total time required for development to maturity under favorable conditions is about 7 to 10 weeks, but starvation, low temperature, etc., may drag out the period much longer. There may, however, be three or four generations in a year. The adults under ordinary conditions usually live for several months to a year or more.

Effects of Bites. The degree of irritation caused by bites of bedbugs undoubtedly depends to a large degree on development of hypersensitivity or eventual immunity (see p. 511). The irritation is produced by the salivary secretion, but when an engorging bug is undisturbed much of the secretion is redrawn with the blood meal and the irritation is lessened. Continued excessive biting by bugs may cause anemia, nervousness, insomnia, and general debility. Titschack found that the bites of 50 adults were enough to produce influenza-like symptoms, whereas over 100 caused palpitation of the heart, headache, and eye

disturbances. Hase (1938) considered these eye disturbances to be a fairly common phenomenon when numerous bugs bite day after day.

Bedbugs and Disease

General Considerations. The bedbug would appear at first sight to be eminently adapted for human disease transmission. Like an ex-criminal, it is under constant suspicion. With or without reason it has been on trial in connection with kala-azar and other forms of leishmaniasis, relapsing fever, leptospirosis, South American trypanosomiasis, leprosy, plague, typhoid, infantile paralysis, some filaria infections, seven-day fever, typhus, tularemia, yellow fever, and even malaria and beri-beri. In spite of all this suspicion and some circumstantial evidence there is still to be produced any single instance in which the bedbug has been shown to be more than a relatively unimportant accessory in the transmission of any human disease.

Of the numerous pathogenic organisms mentioned above, none except leptospirosis (from guinea pig to guinea pig) has been shown to be transmitted by the bites, although a number of them can be transmitted by inoculation of crushed bedbugs, or by the feces. One factor which limits the effectiveness of bedbugs as disease transmitters is their tendency to stay at home. Although frequently carried about in clothing, they normally live in the homes and not on the persons of their hosts, and they would therefore usually be limited in the spread of a disease except in theaters, hotels, tourist courts, sleeping cars, etc.

Patton's observation in India in 1907 that *Leishmania donovani* underwent multiplication and development in the alimentary canal of bugs fed on patients (see p. 137) led to years of fruitless efforts to establish the bedbug as a transmitter of kala-azar, but it finally had to be admitted that the bedbug plays no appreciable part in the epidemiology of either this disease or of Oriental sore. There seems to be no specificity in the relation between bedbugs and species of *Leishmania* or *Leptomonas*; even *L. ctenocephali* of fleas will develop in them.

The relation of bedbugs to the transmission of *Trypanosoma cruzi* is of the same nature. According to Brumpt these trypanosomes develop in about 80 per cent of bedbugs fed on infected mice, but as a rule these bugs remain infected for a much shorter time than triatomids. There is no evidence that bedbugs play any appreciable role in the transmission of this disease in nature, although a related trypanosome of bats is claimed by Pringault to be transmitted by the bites of *Cimex pipistrelli*.

In a few instances relapsing fever has been transmitted to animals by bugs that had immediately before fed incompletely on infected

animals, a method of transmission which is no more significant than the equally successful experiment of infecting an animal by pricking it with an injection needle that has just been inserted into an infected animal. Bedbugs may harbor both louse-borne and tick-borne strains of relapsing fever spirochetes for several weeks, but they do not transmit them unless a bite or scratch is contaminated by their crushed bodies. Further accusations against the bedbug as a primary factor in the dissemination of relapsing fever appear to be out of order.

Most attempts to transmit leptospirosis by the bites of infected bedbugs have failed, but Blanchard and his colleagues claim to have accomplished this, between guinea pigs, by the bites of infected *Cimex lectularius*, some of which remained infective for over a month. The infection is easily transmitted by inoculating with crushed bugs.

Experiments in Brazil showed that the virus of yellow fever is present in the feces of bedbugs for several days after an infective feed and that these feces are infective when inoculated into monkeys, but there is nothing to suggest that bedbugs play any role in the transmission of yellow fever in nature.

Since the gut of bedbugs, as of many other insects, contains antibacterial substances, few bacteria succeed in establishing themselves in bugs. An exception is the bacillus of tularemia, *Pasteurella tularensis*; bugs fed on infected animals retain virulent organisms in the gut for life. The feces are infective, but the bugs do not transovarially transmit this bacillus. Bacot has shown that plague organisms, also, may develop in bugs though more slowly than in fleas and with a much higher mortality for the bugs. Bugs may possibly play a minor role in human plague.

Another bacterial disease shown by Tovar in 1947 to be transmitted by bedbugs as well as by fleas and ticks is undulant fever or brucellosis. Arthropods fed on infected animals transmitted the disease to other animals when biting, and they may play some part in spreading the disease among animals and from animals to man.

Bugs have also been "among those mentioned" in connection with leprosy, typhoid, and typhus, but the evidence is not sufficient to warrant much excitement over the danger. Probably they will be suspected of carrying many other diseases when other obvious transmitting agents are not discovered. In one epidemic of seven-day fever in the Sudan, for instance, since there was no evidence implicating other bloodsucking insects, the bedbugs, which were abundant in the barracks of the afflicted soldiers, were assumed to be responsible. Such evidence is, of course, entirely inadequate. Many epidemiologists would do well to read more detective stories and learn that the most obvious explanation is often not the correct one.

Remedies and Prevention

Prevention of "bugginess" consists chiefly in good housekeeping, but occasional temporary infestations are likely to occur in almost any inhabited building; often the bugs gain entrance with second-hand furniture, laundry, visitor's luggage, etc. Bedbugs are easily controlled by lightly but thoroughly spraying 5 per cent emulsions or 2.5 per cent suspensions of DDT or 1 per cent Lindane on infested mattresses, bed frames, infested wall surfaces, or furniture. The residual effect is good for 3 to 6 months. For theaters, hotels, etc., power sprayers should be used.

OTHER PARASITIC BUGS

Triatominae

Most of the other true bugs which may be looked upon as normally human parasites belong to the subfamily Triatominae, which comprises members of the large family of predaceous bugs, Reduviidae, which have become addicted to sucking blood from vertebrates instead of

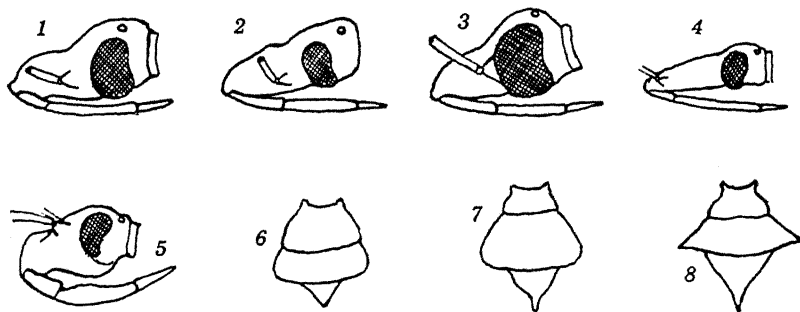


FIG. 181. Heads and thoraces of various genera of triatomids and reduviids. 1 and 2, *Triatoma* (*T. protracta* and *T. rubida*); 3, *Panstrongylus* (*P. megista*); 4, *Rhodnius* (*R. prolixus*); 5 and 6, head and thorax of *Melanolestes*, a reduviid; 7, thorax of *Triatoma*; 8, thorax of *Eratyrus*. (1-4, 7, 8 adapted from Pinto, *Bol. Biológico*, 19, 1931.)

juices from captured insects. Morphologically they differ from the predaceous reduviids in having a slender straight beak instead of a coarse curved one, and in having the antennae inserted on the sides of the head somewhere between the eyes and the end of the "snout" instead of on top of the head (see Fig. 181).

These bugs, of which there are nearly 100 species, are large and often brightly colored, and are active runners and good fliers. They are especially numerous in the warmer parts of the New World, from the

southern half of the United States to Argentina; but one species, *Triatoma rubrofasciata*, is cosmopolitan, and there are a few Old World species. Most of the species live in the nests or burrows of rodents or other animals on which they feed, but a few species have become household pests and feed primarily on man and his household pets, or on the pigs in his yard.

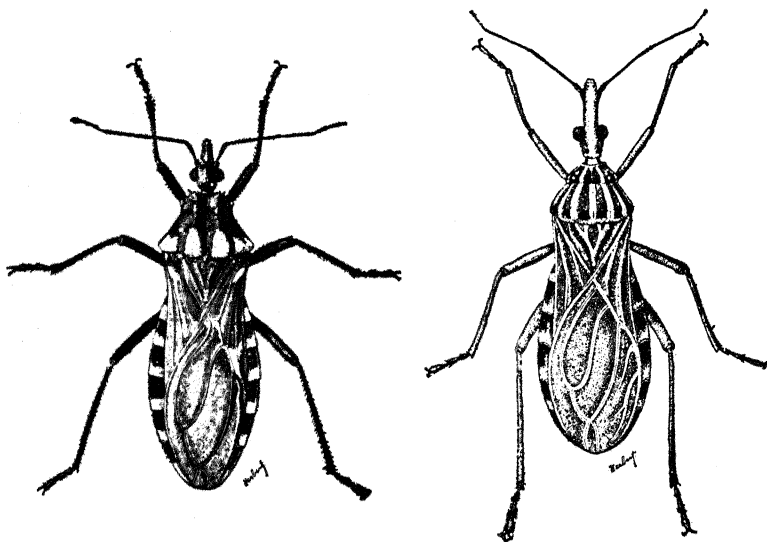


FIG. 182. Left, *Panstrongylus megistus*; right, *Rhodnius prolixus*. $\times 2$. (After Brumpt, *Précis de parasitologie*, 1949.)

The head of triatomids is small and narrow. The slender beak, bent straight back under the head, is three-jointed, and the long filamentous antennae are four-jointed. The pronotum flares posteriorly and is usually fairly distinctly divided into an anterior and posterior lobe; the posterior angles of the latter may be round or pointed (see Fig. 181, 7 and 8). Behind the pronotum is a triangular scutellum which may have a posterior spine. The abdomen has flattened lateral margins, the connexiva, not covered by the wings (Fig. 182). This and the leathery basal portion of the wing (corium) is usually marked with red or yellow, as is the pronotum.

The bloodsucking habit of the Triatominae is probably a recent experiment on the part of these bugs, evolutionarily speaking, for some of them still sometimes pursue bedbugs and are cannibals on each other, obtaining their blood second-hand by sucking it out of their brothers and sisters. The bites of triatomids are usually much less painful than

those of many non-bloodsucking Hemiptera, but in some individuals they may cause severe allergic symptoms. The bites of other reduviids are usually more severe. The triatomids are of great importance because they are the natural and only important transmitters of *Trypanosoma cruzi*.

Genera and Species. According to Usinger (1943) there are nineteen genera of triatomids in the Americas, but some of these contain species which are of no interest here. Used in separating genera are the place of insertion of the antennae, the shape and other characters of the prothorax and scutellum, and hairiness of the body.

The important genera of American Triatominae, and of other Reduviidae which occasionally cause painful bites, can be distinguished by the following key:

Reduviidae (other than Triatominae): Beak thick and curved; antennae inserted just in front of eyes on top of head; head relatively short (Fig. 181, 5).

- 1a. A cogwheel-like ridge on pronotum (wheelbug) *Arilus*.
- 1b. No cogwheel ridge 2.
- 2a. Thorax constricted at or anterior to middle; color nearly uniformly dark brown *Reduvius*.
- 2b. Thorax constricted behind middle (Fig. 181, 6) 3.
- 3a. Wings and body all black or dark brown *Melanolestes*.
- 3b. A large yellow spot on wings *Rasahus*.

Triatominae: Beak slender and straight; antennae inserted on sides of head; head elongated in front of eyes; thorax constricted anterior to middle; black or brown with red or yellow markings.

- 1a. Antennae inserted near apex of head, which is somewhat widened apically (Fig. 181, 4, 196B) *Rhodnius*.
- 1b. Antennae inserted just in front of eyes (Fig. 181, 3) 2.
- 1c. Antennae inserted about midway between eyes and apex of head (Fig. 181, 2) 3.
- 2a. Body clothed in long curved hairs *Parastrongylus*.
- 2b. Body nearly naked *Panstrongylus*.
- 3a. Scutellum with a long pointed spine posteriorly and pronotum with pointed posterior angles (Fig. 181, 8) *Eratyrus*.
- 3b. Scutellum without long spine; angles of pronotum rounded (Fig. 181, 7) body ½ to 1 in. long, distinctly colored *Triatoma*.

Most triatomids will feed on a great variety of hosts, although some are especially associated with certain animals, particularly pack or wood rats (*Neotoma* spp.), armadillos, and opossums. They will feed to repletion on lizards also, and lizards frequently eat the bugs. A few species, discussed below, habitually live in human habitations, in the daytime hiding like bedbugs in the cracks of walls, in thatched roofs, debris on the floor, etc., issuing forth at night to feed on their sleeping

hosts. Most species are so active and hide so rapidly when a light is produced that they are hard to catch. It is probable that any of them would accept a human meal if the opportunity presented itself, but their habits and habitats render some species much more frequent human biters than others.

Life Cycle. The life cycle of triatomids is similar in general to that of bedbugs. The eggs are white oval objects when first laid, in some species turning yellowish or pinkish later; they are laid singly or in small batches by most species, but *Rhodnius prolixus* lays them in a mass joined together by a secretion. The total number laid by a female (not a single female as some writers say—they have to mate!) is usually about 100 to 300. The eggs require 2 to 3 weeks to hatch, the time depending on temperature. The wingless nymphs are light in color when they first hatch but soon darken. They molt a total of five times, always after a full blood meal, which is six to twelve times their own body weight! The later nymphal instars have the wings represented as rounded lobes (Fig. 184B). The whole development from egg to adult requires about a year in some species and 2 years in others.

Important Species. Comparatively few species invade houses and become human pests. In South America three species are of outstanding importance. *Panstrongylus megistus* (Fig. 182A), the “barbeiro” of Brazil, a large, handsome red-trimmed black insect widely distributed in Brazil and neighboring countries, is one of the principal vectors of Chagas’ disease. It is thoroughly domestic in its habits and normally lives in the huts of natives. *Triatoma infestans*, known in Argentina as the “vinchuca,” replaces this species farther south and west as a house-infesting pest. This is the species whose habits were vividly described by Darwin in his *Voyage of a Naturalist*. In northern South America *Rhodnius prolixus* (Fig. 182B) is the most annoying domestic species. This bug is garbed in brown and yellow. Although a common pest in human habitations, it also inhabits burrows of armadillos and pacas.

Other species that breed in houses and are partially “domestic” are *T. braziliensis* and *T. sordida* in South America, *T. dimidiata* in Ecuador, Central America and Mexico; and *Panstrongylus geniculatus*, a species usually partial to armadillos, in Panama.

The cosmopolitan *T. rubrofasciata* is semi-domestic in habits. Many other species frequently enter human habitations to bite if not to breed. Most of the species in the United States, ten of which have been found to harbor *Trypanosoma cruzi* (see p. 167), are commonly found associated with wood rats (*Neotoma*) or in nests of opossums or burrows of armadillos. The adults particularly are likely to invade barns, tents,

or houses or to prowl about in the beds of outdoor sleepers. They are found throughout the southern half of the United States but are especially common in Texas, New Mexico, Arizona, and southern California. The species most often found invading houses are *T. gerstaeckeri* in Texas, which sometimes invades in great numbers; *T. rubida* (= *uhleri*), *T. protracta* (Fig. 183), and *T. recurva* (= *longipes*), found farther west and in Mexico; and *T. sanguisuga*, throughout the South.

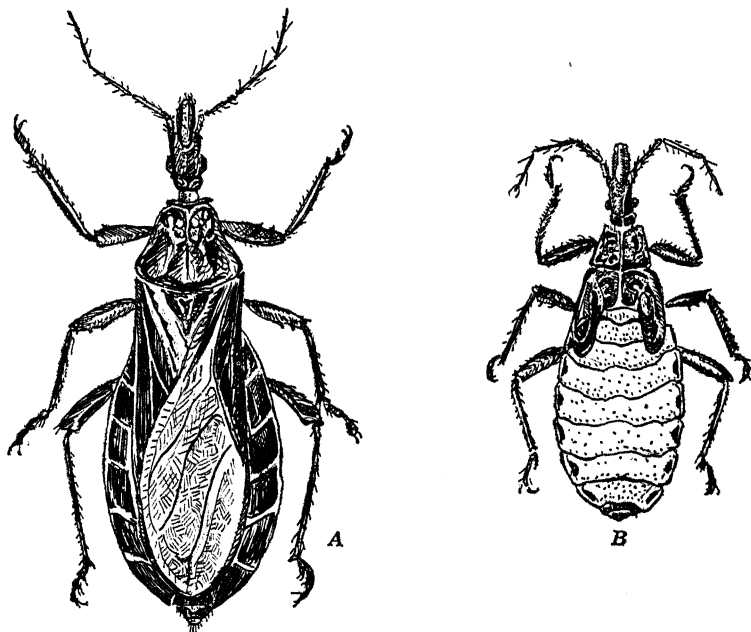


FIG. 183. *Triatoma protracta*, adult and nymph. (Adapted from Usinger, *Publ. Health Bull.* 288, 1944.)

Other Hemiptera

Several reduviid bugs, which are not normally bloodsuckers, often bite man when provoked, and their bites, as noted previously, are far more painful and toxic than those of the true bloodsuckers. In North and Central America there are a number of species of "kissing bugs" and "corsairs" of the genera *Melanolestes*, *Reduvius*, and *Rasahus*. The common kissing bug or black corsair, *Melanolestes picipes*, became very abundant in the United States at one time and gave opportunity for many startling newspaper stories. The wheelbug, *Arilus cristatus*, is another vicious biter.

All Hemiptera have piercing mouth parts and many are capable of inflicting painful wounds, so it is safest not to handle any of them with the bare hands. Although the majority of the bad biters belong to the Reduviidae, the malodorous pito bug, *Dysodius lunatus*, of South America is worthy of mention. It is a broad, flat bug belonging to the family Aradidae; it frequents houses and bites severely. Among other species that bite when handled are various kinds of water bugs. The large "electric light bugs" are venomous enough to kill fish and even birds and to cause in man severe pain lasting for several days.

Triatominae and Disease

At least thirty-six of the hundred or more species of Triatominae have been found to be capable of acting as intermediate hosts of *Trypanosoma cruzi* or a species which is morphologically indistinguishable from it. *Panstrongylus megistus*, *Triatoma infestans*, and *Rhodnius prolixus* are the most important natural transmitters of the disease to man, but *T. dimidiata* and several other species are also important in some localities from Mexico to Ecuador. Species of the genus *Rhodnius* are vectors of *Trypanosoma rangeli* also (see p. 174). *Panstrongylus megistus* seems to be the species most frequently involved in human transmission in the greater part of Brazil. In southern and western Brazil, Uruguay, Argentina, Paraguay, Bolivia, and Chile, *Triatoma infestans* plays the leading role, whereas in northern South America and Central America *Rhodnius prolixus* is the principal vector.

In the United States 10 species of *Triatoma* have been found naturally infected—*gerstaeckeri*, *protracta*, *protracta woodi*, *rubida*, *recurva*, *sanguisuga*, *neotomae*, *uhleri*, *lecticularius*, and *ambigua*. Packchianian in 1939 reported the heaviest infections—92 out of 100 *gerstaeckeri* collected in a house and barn in southern Texas and 65 per cent of *lecticularius* collected at Temple, Texas.

Rhodnius spp. are transmitters of *Trypanosoma rangeli* (= *T. ariarii*) also (see p. 174). Unlike *T. cruzi*, this trypanosome is transmitted by the bite as well as by fecal contamination. *Rhodnius* often harbors mixed infections of *T. rangeli* and *T. cruzi*. Trypanosomes of the African type (*T. equinum* and *T. gambiense*) survive in triatomids for only a short time.

There are certain habits of Triatominae that are of interest in connection with the transmission of trypanosomes. Cannibalism is a common habit among many of them. Young bugs, especially, often suck blood from the distended bodies of nest mates, and they sometimes suck blood from bedbugs. The robbed bugs seem quite untroubled and unharmed by it. Perhaps like the Romans of old they are glad to be

rid of their meals in order to enjoy the ingestion of more. *Rhodnius* is said to feed upon the excreta of fellow bugs. In these ways and perhaps by contamination from feces, *Trypanosoma cruzi* may occasionally spread from bug to bug, but transovarial transmission does not occur. The percentage of infected bugs steadily increases with age up to the adult stage. Infection is usually acquired from infected mammalian hosts, or from lizards (see p. 168).

Since Chagas' disease is transmitted by contamination of bites by feces of the bugs or by rubbing the feces into the eye, species that are quick to defecate while feeding are the only important transmitters. The rare occurrence, if not complete absence, of Chagas' disease in the United States may be due to failure of species that are not habitually domestic, such as *T. protracta*, to defecate while feeding.

In India and also in South America *Triatoma rubrofasciata* is a vector of a trypanosome of rodents, *T. conorrhinae*. In Mauritius, *T. rubrofasciata* has been found to harbor rickettsia-like bodies which were transmissible to laboratory animals. Spirochetes of relapsing fever persist in triatomids for some time, and in Kansas the virus of western equine encephalomyelitis has been isolated from *T. sanguisuga*.

Control

Spraying houses with BHC or Dieldrin is very effective in controlling the house-infesting species. Spraying with 5 per cent emulsions, suspensions, or kerosene solutions controls triatomid infestations even up to a year. The town of Bambui, State of Minas Gerais, Brazil, was entirely freed of triatomids by repeated applications of insecticides in the houses, and there were no new cases of Chagas' disease for over 5 years.

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See also References, Chapter 8.

• 26 •

Lice (Anoplura and Mallophaga)

Opinion is divided as to whether the sucking lice of mammals and the chewing lice of birds and mammals should be placed together in one order Anoplura, the former in a suborder Siphunculata and the latter in a suborder Mallophaga, or should be placed in separate orders Anoplura and Mallophaga, respectively. They have many features in common, but differ in the radically different structure of the mouth parts. Both are small, wingless, flattened insects, probably derived from the free-living book lice or bark lice, Psocida. Although probably they came from the same original stock, they form clearly defined groups with no intermediate forms, so it is convenient to consider them as separate orders.

The Mallophaga are mainly bird parasites, although many of them also make themselves at home in the fur of mammals. They have nipper-like mandibles fitted for nibbling on feathers, hair, and epidermal debris, although some of them quite regularly dine on blood by piercing the pulp of young growing feathers or even gnawing through the skin of the host, but many are apparently content with parts of feathers or epidermal debris. The Anoplura, on the other hand, have piercing mouth parts consisting of three "piercers" which when not in use are drawn back into a special pouch under the pharynx. These feed entirely on blood. Mallophaga annoy their hosts principally by irritating the skin surface, but those that also suck blood (members of the suborder Amblycera) are also potential disease transmitters. The sucking lice cause trouble by sucking considerable amounts of blood, by causing allergic reactions by their bites or feces, and by transmitting disease.

The lice of these two orders are readily distinguishable by the presence in the Mallophaga and absence in the Anoplura of heavily chitinized mandibles which are brown or blackish. They can also be distinguished at once by the fact that the Mallophaga have very broad heads, always at least as broad as the thorax (Fig. 184), whereas in the

Anoplura the head is always narrower than the thorax (Fig. 187). None of the Mallophaga are human parasites but some are annoying to domestic animals, particularly poultry. They are briefly considered on pp. 613-617.

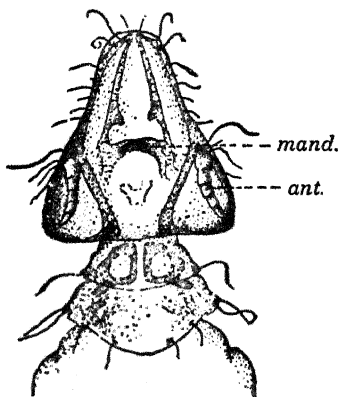


FIG. 184. Head of a species of Mallophaga (*Uchida* sp.) from golden eagle. Note breadth of head compared with thorax, and pair of black-tipped mandibles; ant., antenna; mand., mandibles.

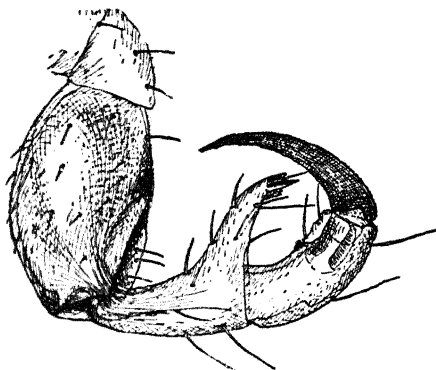


FIG. 185. Front leg of ♂ body louse, *Pediculus humanus*. Note huge claw and thumb-like opposing process of tibia. $\times 100$.

ANOPLURA

Morphology and Physiology. The Anoplura have the body clearly divided into a narrow and often elongate head, a broad thorax, the segments of which are fused in nearly all species, and an abdomen that is more or less distinctly divided into segments (Fig. 187). There are primitively nine segments, but one or two of the anterior ones are fused or lost, so usually seven or eight are recognizable. In the crab louse, *Phthirus*, segments III to V are fused. Ordinarily segments III to VIII bear spiracles, and there is one pair of spiracles on the thorax also (two pairs in a family of lice on seals). The abdomen of lice is poorly chitinated except for the pleural plates at the sides in some genera, e.g., *Pediculus*. In the females the terminal segment of the abdomen is indented, whereas in the males it is rounded, with the large spike-like vaginal dilator often projecting from the dorsally situated sex opening just posterior to the anus.

The head has short three- or five-jointed antennae; eyes are absent in most species, but the human lice have small but prominent ones. The legs, except in one genus found on elephants, have each tarsus,

consisting of one segment, armed with a large curved claw, quite grotesque in appearance in some species, which closes back like a finger against a thumb-like projection of the tibia (Fig. 185). There are not even rudiments of wings.

The mouth parts (Fig. 186), fitted for piercing and sucking, are so highly modified that their homology is in doubt. There is a short tubular haustellum (*h.*) armed with teeth which can be everted so that the teeth are on the outside, as shown in the figure. This appressed to

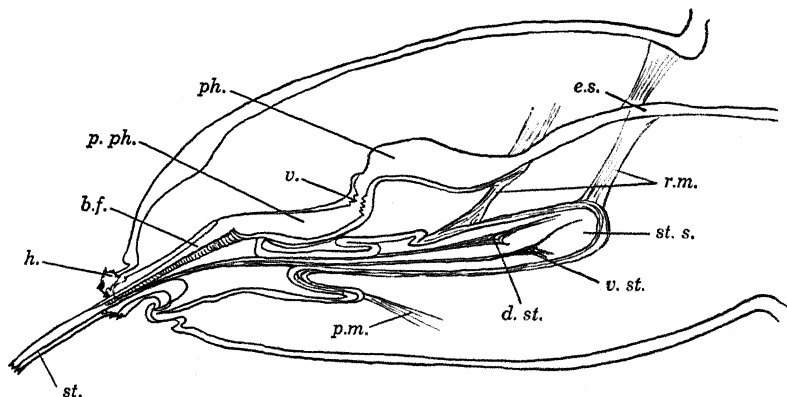


FIG. 186. Mouth parts of *Pediculus humanus*; *b.f.*, buccal funnel; *d.st.*, dorsal stylet; *e.s.*, esophagus; *h.*, haustellum (everted); *p.ph.*, prepharynx; *ph.*, pharynx; *p.m.*, protractor muscle; *r.m.*, retractor muscles; *st.*, stylets; *st.s.*, stylet sac; *v.*, valve; *v.st.*, ventral stylet. (From Sikora, *Centr. Bakt.*, 1, Orig., 76, 1915.)

the skin makes a tight seal. Through this can be protruded three slender stylets which, when not in use, are retracted into a blind sac lying under the pharynx. The dorsal and ventral stylets are forked at their proximal ends in the stylet sac. The ventral stylet is believed by Ferris (1951) to represent the terminal part of the labium, the more basal part forming part of the floor of the stylet sac. This stylet is stouter than the others and toothed at the tip, and used for piercing the skin. In a groove on its dorsal surface lies the extremely slender middle stylet, a hypostome, at the tip of which the salivary duct opens. The dorsal stylet, partly embraced by the ventral one, is believed by Ferris to represent fused maxillae. It has a groove which Buxton (1947) and others believe acts as a food channel, although Ferris denies this.

The stomach is provided with lateral pouches in order to increase the food capacity. Normally lice do not fill themselves to repletion and then wait until this food is digested before feeding again but enjoy more moderate meals several times a day.

All except the human body louse glue their eggs to hairs near the base. The eggs hatch in a few days, and the young nymphs closely resemble the adults except for their size and paler color. There are three nymphal instars; the third molt brings them to the adult stage in 10 to 20 days.

Most species of lice are quite closely limited to a single host, and sometimes even genera are thus limited. Kellogg has suggested that the evolutionary affinities of different birds and mammals may be demonstrated by the kinds of lice that infest them. Only about 230 species of Anoplura are known, but the species of Mallophaga are numerous. Ferris (1951) divides the Anoplura into several families as follows:

- 1a. Abdomen without any sclerotized plates except on terminal and genital segments 2.
- 1b. Abdomen with pleural plates (paratergites), and usually tergal and sternal plates also 4.
- 2a. Body robust, and bristly or spiny; legs, at least last 2 pairs, with very stout undivided tibiotarsus; on seals **Echinophthiriidae.**
- 2b. Body with setae but not spines; 1st pair of legs smaller than 2nd or 3rd. 3.
- 3a. Abdominal spiracles several; on Artiodactyla and hyraxes. **Linognathidae.**
- 3b. Only 1 abdominal spiracle, on 8th segment, on shrews. **Neolinognathidae.**
- 4a. Pleural plates (paratergites) with their apical parts projecting free from body; legs all about equal, or 1st pair smaller; majority on rodents, a few on insectivores and primates, one on Equidae **Hoplopleuridae.**
- 4b. Pleural plates without free apices 5.
- 5a. Eyes reduced or absent, legs and claws approximately alike on all 3 pairs; on Artiodactyla and Equidae **Haematopinidae.**
- 5b. Eyes with well-developed lenses and pigment; legs all about equal, or 1st pair smaller; on Primates, including man **Pediculidae.**

Human Lice

In former times human lice were looked upon with less disgust and loathing than they are in most civilized countries now. In days when a bath on Saturday nights (except in winter) was considered adequate and most laundering was done on river banks, lice intruded themselves in everyone's company, from the royal family to the lowest peasant. Even today, however, body lice are distressingly common in camps, jails, trenches, etc., where association with careless people cannot be avoided and facilities for cleanliness are not all that could be desired, especially in time of war. In some parts of the world lice are believed to be indicative of robust health and fertility. Head lice are even more prevalent among the poorer classes in cities, particularly among children. A survey in England in 1939-1940 showed that in industrial cities 50 per cent of preschool children and of school girls harbored them. In women the incidence never fell under 5 to 10 per cent,

and in young women in industrial areas it was 30 to 50 per cent. Permanent waves tend to bring lice more peace and quiet in the heads of young women. The incidence was only 2 per cent in men, and relatively rare (under 5 per cent) in rural areas, where lousiness is considered a disgrace.

The lice infesting man belong to two genera, (1) *Pediculus*, including the head and body lice, and (2) *Phthirus*, with only a single species, the crab louse. Ferris (1951) recognized only four species of *Pediculus*: *P. mjöbergi* on American monkeys; *P. schäffi* on the chimpanzee; *P. pseudohumanus* on American monkeys and man in Central America and the South Pacific (a doubtful species); and *P. humanus* on man. The last species has two biological varieties, one inhabiting the head and known as *P. humanus humanus*, the other normally living on clothing and known as *P. humanus corporis*. During World War I, when lice enlarged their acquaintanceship extensively, the latter were called "cooties" or "graybacks."

No doubt both the head louse and body louse are the descendants of a species that roamed the hairy bodies of our forefathers in the days when we fought our struggle for existence with mammoths and cave bears instead of tax collectors and strike organizers. With the developing hairlessness of the host, the hunting grounds of human lice became more and more restricted. The crab louse adapted itself to the coarse residual body hair, but *P. humanus* solved the problem in two different ways: some retired to the fine hair of the head and became head lice, while others, more resourceful, adapted themselves to living on the clothing next to the skin and became body lice. With the differentiation of the principal races of man some slight differentiation of the head lice may also have occurred; Ewing recognized four varieties, found on Caucasians, Negroes, Chinese, and American Indians, respectively, but other louse specialists do not recognize them. Even if such varieties once existed it would be almost impossible to find pure strains now, for the lice interbreed as do their hosts. Studies of ethnology of lice and of man are beset with the same difficulties.

HEAD AND BODY LICE (*PEDICULUS HUMANUS*)

Morphology. The general appearance of *Pediculus humanus* can be seen from Fig. 187. The head has eyes and five-jointed antennae, the latter distinctly longer in the body than head lice. The thorax has a single pair of spiracles, situated between the first and second pairs of legs. The abdomen is composed of seven segments (III to IX), of which the first six bear spiracles. Pleural plates are well developed, but more so in head than in body lice, resulting in a more festooned

appearance in the head lice. Females, somewhat larger than males, are usually 2.4 to 3.3 mm. long in head lice and 2.4 to 3.8 mm. in body lice. They can readily be distinguished from males by the indented posterior end of the abdomen and by the slenderer anterior legs with smaller grasping apparatus. In males the anus and sex openings are dorsal in position.

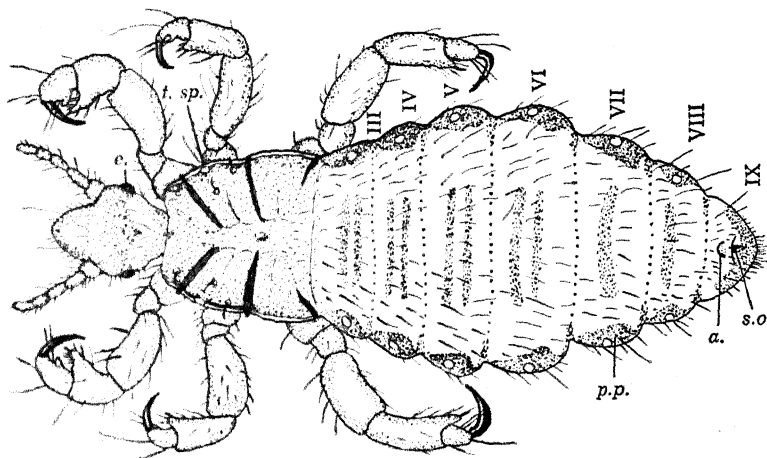


FIG. 187. *Pediculus humanus corporis*, body louse, $\times 40$; a., anus; e., eye; p.p., pleural plate; s.o., sex opening; t.sp., thoracic spiracle; III-IX, abdominal segments. (Adapted from Keilin and Nuttall, *Parasitology*, 22, 1930.)

Biology. Head lice prefer to live in the fine hair of the head, though they sometimes wander to other parts of the body. They occur on all races of man in every part of the world. Buxton found that the majority of infested persons, however, harbor very few lice. In England a high percentage have only 1 to 10, and less than 10 per cent have over 100, usually in girls 5 to 8 years old. Apparently brushing and combing keep them at a low level.

The body louse, on the other hand, lives on the clothing instead of the hair of its host; the German name "Kleiderlaus" is a very appropriate one. Possibly this louse developed independently from the ancestral ape-man louse, shifting its position from the waning hair to the clothes as nudism temporarily went out of style, but more likely it developed from the head louse. It is a true radical in its habits, for of all the lice in the world it alone lives elsewhere than in the hair of its host. A person infested with hundreds of body lice may remove his clothing and find not a single specimen on his body. An examination of the underwear will reveal them adhering to the inside surfaces.

Here they live and lay their eggs, reaching across to the body to suck blood, holding to the clothing by their hind legs.

Life Cycle. The eggs of lice, commonly called "nits," are oval, whitish objects fitted with a little lid at the larger end which is provided with air cells pierced by pores through which air can enter the egg. The eggs of head lice are slightly less than 1 mm. in length, and are glued to the hairs by means of a cement-like excretion (Fig. 188A). The favorite "nests" are in the vicinity of the ears. The average number laid by each female, according to Bacot, is 80 to 100.

Body lice lay slightly larger eggs and glue them to the fibers of the clothing (Fig. 188B), especially along the seams or creases. Under experimental conditions the body louse will sometimes lay eggs on hairs, but it nearly always selects the crossing point of two hairs and shows less skill than the head louse in attaching the eggs. The body louse shows a marked "homing" instinct in laying her eggs, and tends

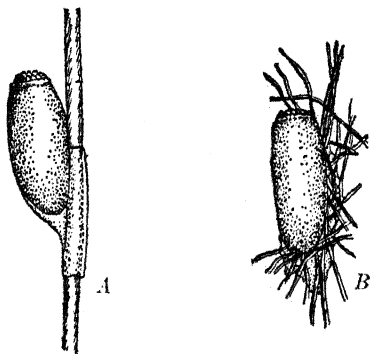


FIG. 188. A, egg of head louse attached to a hair; B, egg of body louse attached to fibers of clothing. $\times 25$. (After Cholodkowsky.)

to cluster them until 50 or 75 have been collected. The total number of eggs may be 200 to 300. The female begins production slowly, but after a week of practice she reaches an output of about 8 or 10 per day, although there is never more than one developed egg in the body at a time. Unfertilized eggs are sometimes laid, but they do not develop. Egg-laying ceases at temperatures below 77°F ., and a daily exposure to a temperature of 60°F . for only 2 or 3 hours causes a marked falling off in egg production.

At 80° to 85°F ., the eggs hatch in about 8 to 10 days; at higher temperatures many die. No hatching occurs below 70°F ., and eggs held below 60°F . for 7 to 9 days do not hatch even if warmed. Either excessive humidity or complete drying is fatal to the eggs. It is evident that in winter the laying off of the clothing at night in a cold room or the leaving of mattresses or bedclothes in the daytime is sufficient to prevent the laying or hatching of eggs.

The young lice have an interesting way of escaping from the eggs. They suck air into the body and expel it from the anus until a cushion of compressed air is formed sufficient to pop open the lid of the egg. The newly hatched lice are almost perfect miniatures of the adults except

that they have three-segmented antennae. They are ready to feed almost as soon as they emerge from the egg and will usually die in less than 24 hours if not allowed to feed. At a temperature of 95°F. and with as many daily feeds as would willingly be taken, namely six, the lice pass through the first molt in 3 days, the second in 5 or 6 days, and the third, which brings them to maturity, in 8 or 9 days. With fewer feeds or lower temperatures the development is slower.

Egg-laying begins 1 to 4 days after the final molt and continues at the rate previously described until the death of the insect. The average length of life for the females is about 35 or 40 days and probably a little less for the males.

Feeding Habits. Lice show less tendency to vacillate in their drilling operations than do fleas. They make a single puncture and then rely on the salivary secretion to dilate the capillaries by its irritation and thus facilitate the flow of blood; this sometimes requires several minutes. They may suck to repletion in a few minutes but often continue to pump blood into their stomachs intermittently for several hours, meanwhile voiding feces containing undigested blood corpuscles.

There seems to be some degree of specificity in the salivary secretion, since it is more efficient in aiding the lice to suck blood from man than from other animals. Rat blood seems to disagree with human lice.

Lice do not have the remarkable resistance to starvation displayed by ticks and bugs. At high temperatures they succumb in 2 or 3 days but at about 40°F. can live for 8 or 10 days without food. Adult lice stand exposure to moderate cold very well but are killed in a few hours at temperatures of 10°F. or below. They are highly susceptible to heat, especially when the humidity is high, and die in a few minutes at 122° to 126°F.

The maximum favorable temperature for the development and reproduction of lice is about 95°F. The absence of lice from hot countries—observable in Mexico, for instance, where they are abundant on the central plateau above 5000 to 6000 ft., but absent from the hot coastal strips—is apparently not due to the high temperature but probably to the disastrous effect of profuse perspiration and consequent excessive humidity between the clothes and skin. Head lice are found in hotter countries than body lice, especially on bareheaded people.

Effect of Bites. The effect of louse bites varies greatly with individuals and with the degree of sensitivity to them, for according to Peck, Wright, and Gant (1943) the principal symptoms appear to be allergic in nature. When persons previously unexposed to lice are experimentally bitten there is at first only a slight sting and little or no itching or redness. After about a week such a person may become

sensitized, and then the bites cause considerable irritation and inflamed red spots. When such persons are bitten by large numbers of lice there may be a general skin eruption, mild fever, and a marked feeling of tiredness and irritability. The bites themselves are only partially responsible; much of the reaction is due to contact of the bites with the feces of the lice, to which infested individuals also become sensitized.

Eventually the increased sensitivity gives way to immunity as with other insect bites (see p. 511), and people long infested become oblivious to them. During the stage of increased sensitivity the irritation leads to scratching, and sometimes the scratched bites become secondarily infected, causing pustules to form. Often areas around the bites turn brown, giving the skin a mottled appearance. In very negligent individuals badly infested with head lice the hair may become matted and form a sort of filthy carapace under which fungus growths develop, and the head may exude a fetid odor.

The interesting observation that white rats that have remained free from lice for years promptly become lousy (probably from wild rats or from a very few they previously harbored) when placed on a diet deficient in riboflavin (one of the vitamin B complex) may possibly have some bearing on the fact that some individuals seem to be attacked more readily than others, and that lice become especially prevalent under conditions of hardship and starvation.

CRAB LOUSE

The crab louse, *Phthirus pubis* (Fig. 189), is quite distinct from the other two species of human lice. It has a very broad short body with long, clawed legs, presenting the general appearance of a tiny crab, from which it derives its name. The first pair of legs are smaller than the others and do not possess a "thumb" in opposition to the curved claw. The thorax is very broad with all the segments fused, and the abdomen is greatly foreshortened. Its first three segments (III to V) are fused into one, which bears three pairs of spiracles. The last four segments bear wart-like processes on the sides, the last pair of which is particularly large. This louse is grayish in color, with slightly reddish legs. The females are about 1.5 to 2 mm. in length, the males somewhat smaller. The favorite haunts are the pubic regions and other parts of the body where coarse hair grows, as in the armpits and in the beard, eyebrows, and eyelashes. Occasionally they infest almost the entire body except the head; the writer once saw a hairy individual who was covered with them from eyebrows to ankles. Unlike the other human lice this species is almost exclusively confined to the Caucasian race.

The females produce 25 or more eggs and glue them, one at a time, to the coarse hairs among which they live. A number of eggs may be glued to a single hair and often at some distance from the skin. The eggs hatch in 6 or 7 days, and the young become sexually mature in about 2 to 3 weeks. This species, even under favorable conditions, can live apart from its host only 10 or 12 hours. The eggs are said not to

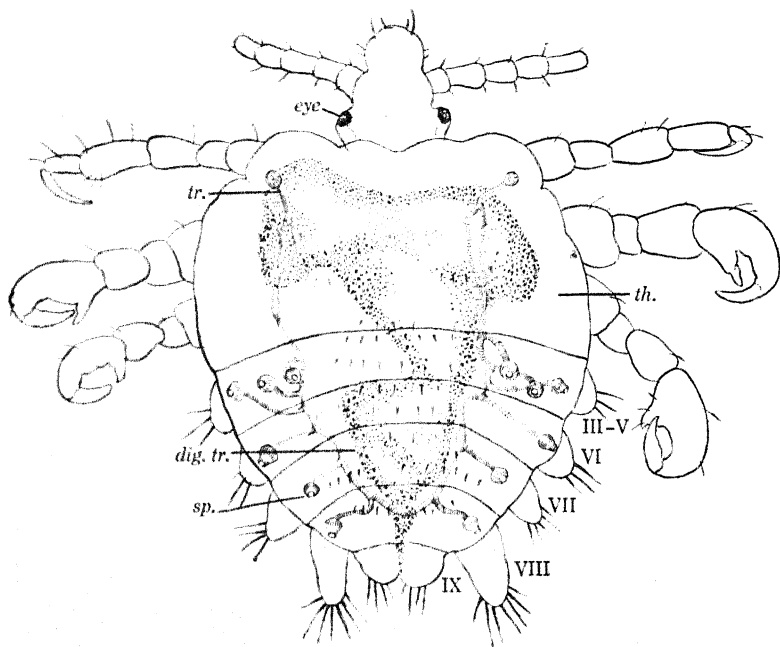


FIG. 189. *Phthirus pubis*, ♀, $\times 35$; dig.tr., digestive tract; sp., spiracle; th., thorax; tr., trachea; III-IX, abdominal segments.

develop except at temperatures between 68° and 86°F., which are approximately the temperatures to which eggs attached to hairs beneath the clothing would be exposed in cool climates. The adults suck blood intermittently for hours at a time, and often cause severe itching. The secretion of one of the pairs of salivary glands has a peculiar effect on hemoglobin, causing it to turn a violet color in the absence of air; in the body this often causes the formation of telltale pale blue spots from $\frac{1}{8}$ to 1 in. in diameter.

Crab lice move about much less than head or body lice, but usually shift their positions daily. The adults probably do not live more than a few weeks. The infestation rate is usually rather low, even when

other lice are common. Since it is very often, though by no means always, venereally transmitted, the French call it the "papillon d'amour."

Lice and Disease

Louse-borne diseases have in the past ranked high among the minor horrors of war—higher, certainly, than they ever will again. In peacetime large louse-borne epidemics do not regularly occur since people and communities are rather sharply divided into those who tolerate lousiness and those who do not. The former are exposed to bites of lice from birth; they suffer from louse-borne diseases early in life, become immune, and are kept immune by repeated reinfection. The louse-free population suffers only sporadic cases since there is not sufficient louse traffic between the two components of a community to cause an epidemic except under disrupted conditions brought on by disaster, famine, or local conditions where facilities for keeping body and clothes clean are inadequate, as in construction camps, prisons, etc. Furthermore, there is ordinarily no opportunity for building up the virulence of the organisms concerned by a rapid sequence of human cases, as happens at the beginning of epidemics.

There are three diseases for which lice are the primary transmitters—epidemic typhus, trench fever, and relapsing fever. The first is caused by *Rickettsia prowazekii* (see p. 227), the second is believed to be caused by another rickettsia, *R. quintana*, and the third is caused by a spirochete, *Borrelia recurrentis* (see p. 53). Lice are certainly not the primary transmitters of either typhus or relapsing fever; epidemic typhus has undoubtedly been derived from flea-borne endemic typhus, and relapsing fever from tick-borne strains. The rat louse, *Polyplax spinulosa*, is capable of transmitting endemic typhus among rats. Typhus organisms are invariably fatal to lice, though unfortunately not quickly enough to prevent transmission, whereas fleas suffer no evident ill effects, and the rickettsias of mites and ticks are even transovarially transmitted. Relapsing-fever spirochetes have become better adapted to lice but are not transovarially transmitted. For a discussion of the interrelations of rickettsias and spirochetes with their various vectors, see pp. 52 and 229.

Epidemic Typhus. Louse-borne typhus, known in Europe for centuries, seldom makes itself evident except in extensive outbreaks during wars or other conditions when, as already noted, lice have an opportunity to extend their acquaintanceships widely and to transmit the organisms to many people who had no chance to develop immunity early in life. Zinsser says that typhus has killed more human beings than any other disease. It was typhus that caused Napoleon to with-

draw his armies from Russia. It is estimated that this disease killed 3,000,000 Russians during World War I. In former days the disease broke out on sailing ships or in prisons so frequently that it was sometimes called ship fever or jail fever. Hence the name epidemic typhus. In New York and Boston, however, and probably elsewhere, the disease exists in endemic form and is called Brill's disease. Some workers believe these cases to be due to individuals harboring the rickettsias for many years, perhaps for life, but von Bormann (1952) has made out a strong case for louse transmission. The majority of the cases occur among people who handle worn clothes, such as tailors and cleaners.

Lice are also able to transmit the endemic or murine strain of typhus, *Rickettsia typhi*, which is normally flea-borne (see p. 633); such louse-borne outbreaks have been reported in Mexico, Spain, Manchuria, and Africa. Ordinarily, at least, *R. typhi* retains its distinctive characteristics even when transmitted by lice.

Epidemic typhus is practically absent from the tropics, e.g., India and tropical parts of Africa and South America, even when lice are abundant. Body lice are the principal disease transmitters, perhaps because head lice and crab lice are less frequently passed around, for these lice experimentally are good hosts for *Rickettsia prowazekii* and *R. quintana* also. Epidemics occur most frequently in winter when people are closely huddled together and the lice nightly migrate from one pile of clothing to another. Lice become infected from typhus patients from early in the disease to about the tenth day or later, even after the temperature has fallen, although by no means all lice become infected. The rickettsias multiply in the epithelial cells, which become greatly distended, and in the lumen of the midgut, and are voided in the feces after a few days. From these time considerations, as Buxton (1947) pointed out, lice from convalescing or dead typhus patients are more dangerous than those from cases at the height of the disease. Transmission results from contamination of the bites or scratches by the feces, or even from inhalation of dried feces; the latter may remain infective for over two months, long after the living lice are gone. A person who wears the boots or clothing of typhus victims may also become a victim.

There is no transovarial transmission. Although, as pointed out previously, the louse-borne rickettsia, *R. prowazekii*, is probably derived from the flea strain, *R. typhi*, and is closely related to it, it is distinguishable in the laboratory by the fact that it fails to cause scrotal swelling and other scrotal reactions in guinea pigs, as does *R. typhi*.

In man epidemic typhus under epidemic conditions is much more

severe than endemic typhus, sometimes causing the death of 70 per cent of its victims. This is doubtless due in part to exaltation of virulence by rapid passage through numbers of susceptible people and in part to lowered resistance under wartime conditions. Poor diet and undernourishment are big factors. The disease is marked by severe headache, prostration, high fever, and a rash caused by small skin hemorrhages. It can be prevented by vaccines and is susceptible to treatment with antibiotics, particularly chloramphenicol and Terramycin. The evidence indicates that these drugs suppress the multiplication of the rickettsias for about a week, by which time the patient will have initiated his own defensive mechanism. With DDT or chlordane to destroy lice, control of typhus is now a relatively simple matter, at least until lice develop resistance to these chemicals, as they have already done in Korea and Egypt. It is unlikely that typhus will ever again cause devastating epidemics in civilized countries.

Trench Fever. It is generally believed that this disease is also caused by a rickettsia, *R. quintana* (see p. 227), which, like the non-pathogenic *R. pediculi*, lives in the lumen of the intestines of lice but not in the epithelial cells. Although unknown previously, this disease became so common during World War I that it caused more sickness than any other disease except scabies. After the war it fell into obscurity again, but an outbreak of what was probably the same disease occurred among louse-feeders in a typhus-vaccine laboratory in Warsaw just prior to World War II, and some small outbreaks occurred in the Balkans during that war. The rickettsia involved in Warsaw was named *R. weiglii*.

The best explanation for this "here again, gone again" disease is, in the writer's opinion, that the supposedly non-pathogenic *R. pediculi*, when lice are restricted to their home-folks, produces mild or inapparent human infections early in life, resulting in immunity, but when the lice get access to numerous previously unexposed and susceptible people, and are passed through a series of these, the rickettsias have their virulence exalted and cause epidemics which subside when normal relations between lice and their perennially infested home-folks are re-established.

The infection is transmitted, like typhus, by louse feces, but since urine and feces of human cases are infective, it may not be spread exclusively by lice. The symptoms are headache, body pains, a double rise of fever, albumin in the urine, and usually a rash.

Relapsing Fever. When lice ingest the blood of a relapsing-fever patient, most of the spirochetes die in the alimentary canal within a very short time, but a few survive by penetrating into the body cavity.

Although very sparse for a few days they become abundant after about a week. Neither the bites nor the feces of the lice are infective, and transmission occurs only by breaking or crushing lice and inoculating bites with the infective body fluid. For further information about relapsing fever and distribution of the louse-borne type, see pp. 53-54. Although louse-borne strains were undoubtedly derived originally from tick-borne infections, lice seem not to be susceptible to some tick-borne strains although they are to others.

Louse-borne relapsing fever shows the same peculiarities of occurrence as typhus; epidemics always rage fiercest in winter and usually break out during wartimes.

Lice and Other Diseases. Lice may also serve as mechanical transmitters of certain other diseases. The bacilli of bubonic plague have been found alive in both body lice and head lice taken from victims of the disease, and both species have been experimentally proved able to transmit plague from rodent to rodent in Java. Lice do not transmit plague by their bites, but they may transmit it when crushed, and possibly with their feces. Natives in Java kill lice by mashing them against the head of the host, which should make infection through the scratched sores on the head very easy. In Ecuador and Peru natives are said to kill lice by crushing them between the teeth; there is much more danger involved when man bites louse than when louse bites man.

Most bacterial diseases are not transmitted by lice except possibly immediately after an infective feed, for most bacteria are destroyed in the alimentary canal by an antibacterial substance. Lice have been suspected of transmitting various diseases just as bedbugs have, but no scientific evidence supports the suspicions.

Prevention and Remedies

Methods of Dispersal. The prevention of lousiness consists primarily in personal cleanliness. However, no amount of personal hygiene and cleanliness will prevent temporary lousiness if there is association with unclean and careless companions. Lousiness and human wretchedness and degradation have always been companions, but this does not imply that lice have any inherent abhorrence of a clean body if they can get access to it. From the nature of their habitats the common modes of infection of the three different species of human lice vary somewhat. The head louse depends for distribution largely on crowded cloakrooms, on promiscuous use of combs and brushes or borrowed hats and caps, and on the free-for-all trying on of headgear in haberdasheries and millinery shops. The body louse is dispersed by clothing and bed linen, usually at night, and finds fresh hunting grounds by

nocturnal migrations from one pile of clothes to another. The crab louse sometimes utilizes public toilets for dissemination and is commonly spread by promiscuous sexual intercourse.

Where men are crowded together in prisons or war camps lousiness is almost sure to develop unless particularly guarded against, since some unclean persons are nearly always in the aggregation, and conditions are such that the infestation is given every opportunity to spread. Even under normal conditions there are many opportunities for dispersal. Buxton (1947) recalls seeing some men sitting on a wall in Iran, catching lice and dropping them into the street, with typhus and relapsing fever epidemic at the time. Of importance in connection with the spread of these diseases is the fact that lice desert a febrile patient and seek a new host. In Europe during World War II lice were mostly well controlled in military forces, but they spread extensively among civilians, especially in crowded bomb shelters and in crowded homes for evacuated children.

Elimination of Lice. Few preventive measures have given more spectacularly good results than the use of DDT in destroying body lice and protecting against them. During the latter part of World War II every American soldier and sailor was provided with a dusting powder consisting of 10 per cent DDT in pyrophyllite and was free of cooties for the first time in any war. The dust was applied by blow-guns to the head, skin, and clothing, without undressing. One pound of DDT powder was enough to dust 15 to 20 persons.

Unfortunately lice in at least two places (Korea and Egypt) have developed resistance to DDT, but other chemicals can be used, especially 1 per cent Lindane or pyrethrum powders. One of the best is MYL powder, containing 0.2 per cent pyrethrins with other chemicals added to give it stability, to reduce allergenic properties, and to kill eggs. It is effective for a week if rubbed into underwear, and can be applied to heads at the rate of 4 grams (about a teaspoonful) per person, more for women. Two or three applications usually give complete control. The DDT does not kill the eggs but remains effective long enough to kill the young lice when they hatch. Reinfestations may come from combs, brushes, schoolmates, or other members of the family. Cold-cream ointments containing DDT, Lindane, pyrethrins, rotenone, or benzyl benzoate, as well as the powders mentioned above, are effective against crab lice. The lice are killed quickly, the itching stops, and the applications can be washed off after 10 or 12 hours.

For disinfection of clothing, hot water, dry heat, pressing with a hot iron, live steam, or laundering in various disinfectant solutions are all effective. Soap containing about 3 per cent DDT is also effective;

it retains 75 per cent of its DDT for a year. Dipping in 5 per cent DDT solution or emulsion renders clothing protective against lice through several washings, and persists long enough to kill young lice as they hatch from eggs. Fumigation with methyl bromide has been used at United States ports of disembarkation for eliminating lice from clothing of prisoners of war.

Anoplura on Domestic Animals

The Anoplura that torment domestic animals belong to the families Linognathidae and Haematopinidae. The latter have well-developed pleural plates, vestigial eyes if any, and all the legs about equal. There

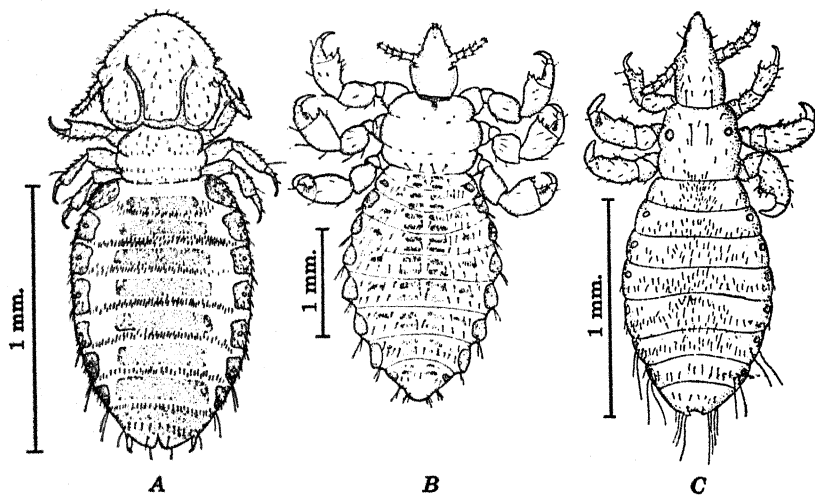


FIG. 190. Cattle lice: A, *Damalinia* (= *Bovicola*) *bovis*; B, *Haematopinus* *eurysternus*; C, *Linognathus* *vituli*. (After Mönnig, *Veterinary Helminthology and Entomology*, Williams and Wilkins, 1949.)

is only one genus, *Haematopinus*, on domestic animals, including *H. suis*, common on pigs; *H. asini* of horses; and *H. eurysternus* (Fig. 190B), the short-nosed louse of cattle, of which *H. quadripertusis*, the tail louse of cattle, may be only a variety.

The Linognathidae, which have no sclerotized abdominal plates, include three genera with important species on domestic animals: (1) *Solenopotes*, with only one row of bristles on each abdominal segment, mostly parasitic on deer but with one species, *S. capillatus*, on cattle; (2) *Linognathus*, with two or more rows of bristles on the abdominal segments and with no eyes, including *L. vituli* (Fig. 190C), the long-

nosed or blue louse of cattle; *L. stenopsis* of goats; *L. pedalis*, the foot louse of sheep; and *L. setosus* of dogs and foxes; and (3) *Microthoracius*, also with numerous bristles, but with very long heads, and eyes present, containing *M. cameli* of camels, and three species on llamas. Two species of the family Hoplopleuridae (see p. 600), *Polyplax spinulosa* and *Hoplopleura oenomydis*, are common rat lice in the United States, and one, *Haemodipsus ventricosus*, is common on rabbits.

Like the Mallophaga (see p. 616) these lice stick closely to their hosts and are usually transmitted only by body contact, though horse lice are spread by blankets, saddles, etc.

The hosts are much more annoyed by these lice than they are by the Mallophaga. Their fur and skin are affected, and they become restless, lose their appetites, and become susceptible to other diseases. Constant licking by cattle produces hair balls in the stomach, and the foot louse of sheep may cause lameness.

Treatment consists of sprays or dips of 0.5 per cent DDT, TDE, Toxaphene, Chlordane, or Methoxychlor; derris or cubé containing 5 per cent rotenone (1 lb. per 100 gallons); or Lindane, 0.05 per cent. For dairy cattle sprays of 0.025 per cent pyrethrum plus 0.25 per cent piperonyl butoxide, or Methoxychlor at 0.5 per cent, are used since the other chemicals accumulate in the milk. For goats and sheep, somewhat lower concentrations are recommended. In winter, dusts containing 1 per cent rotenone, 10 per cent DDT, etc., or 1 per cent Lindane may be substituted to prevent chilling. Sometimes repetition after 14 to 18 days is needed, but usually one treatment is effective for 6 to 8 weeks. If all farm animals were treated three or four times, many of their ectoparasites could probably be exterminated. Lice have been successfully eliminated from hogs by adding 30 mg. per kg. of Methoxychlor to the food for several weeks.

MALLOPHAGA

Morphology. Two characters make it easy to identify Mallophaga: the head as broad as, or broader than, the thorax; and the pair of strongly chitinated, pincer-like mandibles on the ventral side of the head. In most species the second to seventh abdominal segments bear spiracles. The legs are short and all much alike; in the suborder Ischnocera they are fitted for clasping as in the Anoplura, but in the Amblycera, which roam over the body, the tarsi are longer and modified for clinging to smooth surfaces. The Amblycera have short, four-jointed maxillary palpi, but these are absent in the Ischnocera. These two orders differ also in the antennae; in Amblycera these are short and

tucked into grooves as in fleas, whereas in Ischnocera they are longer and free (Fig. 191).

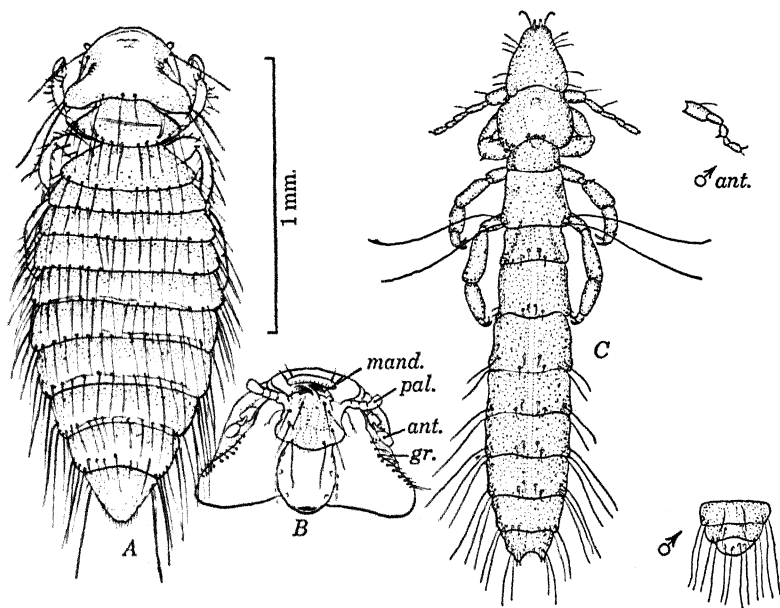


FIG. 191. Examples of two suborders of Mallophaga. A, *Menopon gallinae* of chickens, dorsal view; B, same, ventral view of head (adapted from Ferris, *Parasitology*, 16, 1924). C, *Columbicola columbae* of pigeons, ♀, and antenna and posterior end of abdomen of ♂ (after Martin, *Canad. Ent.*, 66, 1934).

Following is a brief key to some of the families and genera common on domestic animals:

Suborder **Amblycera**. Antennae club-shaped and mostly concealed in grooves; maxillary palpi present (Fig. 191B). Only family important on domestic animals is Menoponidae, infesting poultry.

- A. All tarsi with 2 claws, antennae 4-segmented; head evenly expanded behind and broadly triangular. **Menoponidae** 1.
 - 1a. Thorax with 3 distinct segments (Fig. 192A) *Trinoton*.
2 or 3 spp. on geese, ducks, and swans.
 - 1b. Thorax with 2 segments (Figs. 191A, 192B) 2.
 - 2a. Abdominal segments with 2 rows of bristles *Eomenacanthus*.
E. stramineus (body louse) of chickens.
 - 2b. Abdominal segments with 1 row of bristles 3.
 - 3a. Eye lodged in a shallow sinus (Fig. 191A) *Menopon*.
M. gallinae (shaft louse) of chickens.
 - 3b. Eye lodged in a deep sinus (Fig. 192B) *Colpocephalum*.
C. turbinatum of pigeons and *C. pectiniventris* of geese.

Suborder **Ischnocera**. Antennae filiform and exposed; no maxillary palpi (Fig. 191C).

1. Antennae 5-segmented; tarsi with 2 claws; infesting birds (Fig. 192C-H) **Philopteridae**.
2. Antennae 3-segmented; tarsi with 1 claw (Fig. 190A); infesting mammals **Trichodectidae**.

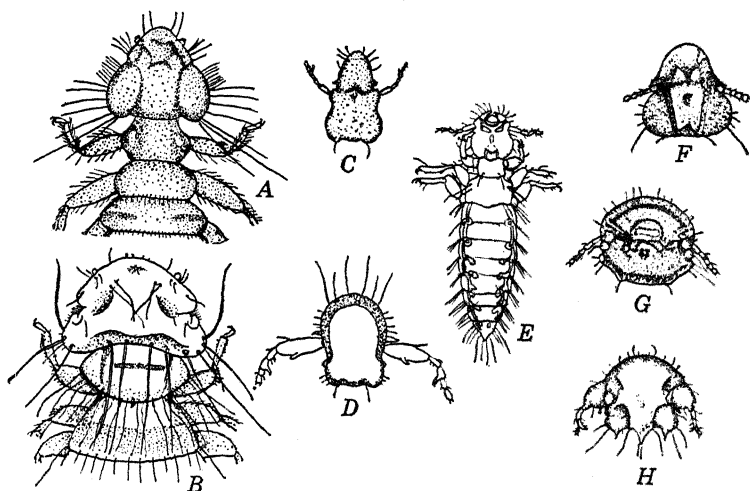


FIG. 192. Details of various Mallophaga to illustrate key. A, *Trinoton querquedulae* of ducks; B, *Colpocephalum pectiniventris* of geese; C, *Esthiopterum crassicornis* of ducks; D, *Lipeurus caponis* of chickens; E, *Ornithobius cygni* of swans; F, *Philopterus dentatus* of ducks; G, *Goniocotes gigas* of chickens; H, *Goniodes pavonis* of peacock. (Adapted from various authors.)

A key to the principal genera of these two families, infesting birds and mammals respectively, is given below, with mention of the commoner and more important parasites of domestic animals in North America:

Ischnocera of Birds (**Philopteridae**)

A. Body long and slender.

- (1) **Lipeurus**: Head nearly hemispherical in front of antennae; in ♂ 1st segment of antenna much enlarged, third segment with prong (Fig. 192D).
L. gallipavonis on turkey; *L. caponis* on chickens.
- (2) **Esthiopterum**: Head elongated in front of antennae; antennae as in (1); clypeus without dorsal spines (Fig. 192C).
E. crassicornis on ducks.
- (3) **Columbicola**: Like (2) but clypeus with 2 pairs of spines dorsally.
C. columbae on pigeons (Fig. 191C).
- (4) **Ornithobius**: ♂ antenna without prongs; abdomen with second chitinized band paralleling chitinized margin (Fig. 192E).
O. cygni on swans.

B. Body broad, abdomen rounded.

- (1) **Philopterus**: Antennae with 5 similar segments in both sexes; a horn-like process in front of insertion of antennae (Fig. 192F).

P. dentatus on ducks.

- (2) **Goniocotes**: No prongs on segments of ♂ antenna; no spine in front of insertion of antennae (Fig. 192G).

G. gigas (3–4 mm. long) and *G. hologaster*, fluff louse, (0.8–1.3 mm. long) on chickens; *G. bidentatus* on pigeons.

- (3) **Goniodes**: Antenna of ♂ with prong on 3rd segment at least; no spine in front of insertion of antennae (Fig. 192H); head angular behind.

G. dissimilis on chickens; *G. damicornis* (2 mm. long) and *G. minor* (less than 2 mm. long) on pigeon; *G. parviceps* (2 mm. long) and *G. pavonis* (3 mm. long) on peacock; *G. meleagridis* on turkey.

- (4) **Cuclutogaster**: Antennae of ♂ with prong on 3rd segment, head rounded behind, without spines.

C. heterographus, head louse of chickens.

Ischnocera of Mammals (Trichodectidae)

A. Damalinia: With pleural plates; antennae alike in both sexes (Fig. 190A).

D. bovis on cattle, *D. caprae* on goats, *D. equi* on horses, *D. ovis* on sheep.

B. Trichodectes: With pleural plates; antennae of ♂ with first segment of antenna enlarged.

T. canis on dogs.

C. Felicola: Without pleural plates; antennae alike in both sexes.

T. subrostrata on cats.

Life Cycle, Habits, etc. The Mallophaga live their entire lives, generation after generation, on their hosts. The Ischnocera are relatively sedentary and feed exclusively, or nearly so, on feathers or epidermal scales. Many stout-bodied species live only on the head where they cannot be picked, other slender forms live on the back or wings. The Amblycera roam about more freely and escape by good broken-field running; most of these, to which the mammalian parasites belong, commonly vary their diet with blood obtained by nipping live feather papillae or nibbling through the skin.

The eggs are glued to feathers or hairs, sometimes in selected places, usually one a day. According to Martin (1933) eggs of the pigeon louse, *Columbicola columbae* hatch in 4 days and the nymphs pass through their three molts and reach maturity in about 3 weeks.

Except for occasional hitchhiking on the bodies of hippoboscids flies, Mallophaga move from host to host only by direct body contact. For this reason they are usually kept in the family and pass from generation to generation of the same species. Thus isolated zoologically, many species and even genera have arisen which are closely confined to particular kinds of birds. They tend to change more slowly than their hosts, so even after their hosts have become widely separated and isolated, and have developed into new species or genera, they may

harbor the same lice as did their remote ancestors. Strong host specificity keeps lice from transferring their attentions to unrelated species even when there is opportunity, e.g., from a goldfinch to a cuckoo, or from a quail to a falcon.

Control. Control of Mallophaga on larger animals is the same as for Anoplura (see p. 613). On chickens, lice can be eliminated by putting pinches of sodium fluoride dust or 5 per cent DDT dust on head, back, vent region, and under the wings, or by painting the roosts with 1 per cent Lindane emulsion or 40 per cent nicotine sulfate.

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- See also References of Chapters 4, 10, and 22.

. 27 .

Fleas (Siphonaptera)

David Harum says, "A reasonable amount of fleas is good for a dog. They keep him from broodin' on bein' a dog." A goodly supply of fleas might likewise keep man from brooding over anything deeper than the presence of these fleas, but in some cases this in itself is a rather serious thing to brood over. Not only are fleas very annoying pests and a common cause of insomnia, but they may also serve as the disseminators of two important human diseases, bubonic plague and endemic typhus.

General Structure. Fleas, constituting the order Siphonaptera, are believed by most entomologists to be more or less distantly related to the Diptera. Their bodies are much compressed to facilitate gliding between the hairs or feathers of their hosts. The head is broadly joined to the thorax, which is relatively small. The abdomen consists of ten segments, the last three of which are modified for sexual purposes, particularly in the male. The first segment is protected by a dorsal plate (*tergum*) only, the second to seventh each by a dorsal tergum and a ventral *sternum* (Fig. 193). In both sexes the tergum of the tenth segment has a pitted area covered with little bristles, called the *pygidium* or *sensillum*. The seventh tergum in most fleas bears one to four pairs of long *antepygidial bristles*.

All parts of the body are furnished with backward-projecting bristles and spines which aid the flea in forcing its way between dense hairs and prevent it from slipping backward. The efficiency of these spines is apparent when one attempts to hold a flea between his fingers. Many fleas have specially developed, thick, heavy spines arranged in rows suggestive of the teeth of combs and therefore known as *ctenidia* or "combs" (Fig. 197). There may be a *genal ctenidium* along the ventral margin of the head, or a *pronotal ctenidium* on the hind margin of the pronotum (the dorsal plate covering the first segment of the thorax), or in both places; a few fleas also have an abdominal ctenidium.

The presence or absence of these combs and the number of teeth in them are of considerable use in identification of species.

The legs of fleas are very long and powerful and at first glance seem to possess one more segment than do the legs of other insects. They

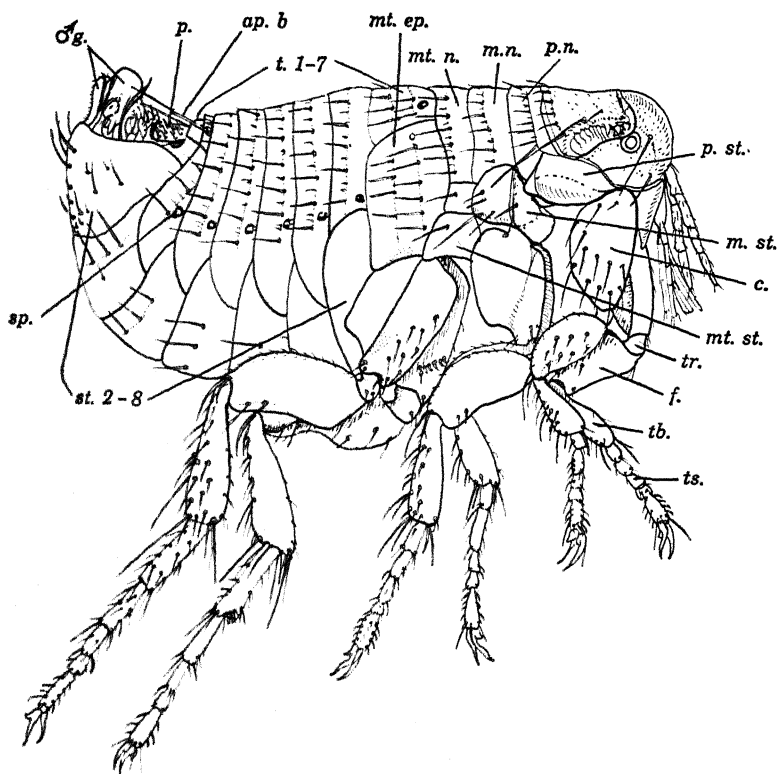


FIG. 193. *Xenopsylla cheopis*, rat flea, ap.b., antepygidial bristles; c., coxa; f., femur; m.n., mesonotum; m.st., mesosternum; mt.ep., metepimeron; mt.n., metanotum; mt.st., metasternum; p., pygidium; p.n., pronotum; p.st., prosternum; sp., spiracle; st. 2-8, abdominal sternites 2-8; t. 1-7, abdominal tergites 1-7; tb., tibia; tr., trochanter; ts., tarsus; ♂g., male genitalia. (Modified from Jordan and Rothschild, *Parasitology*, 1, 1908.)

really consist of the usual number of segments with five-jointed tarsi, but are peculiar in the enormous development of the coxae, which in most insects are quite insignificant (Fig. 193). The shape of the sternal plate to which the coxae are attached is suggestive of still another segment. The great development of the coxae as well as of the other segments of the leg gives unusual springiness and consequently enormous jumping power. The human flea, *Pulex irritans*, has been

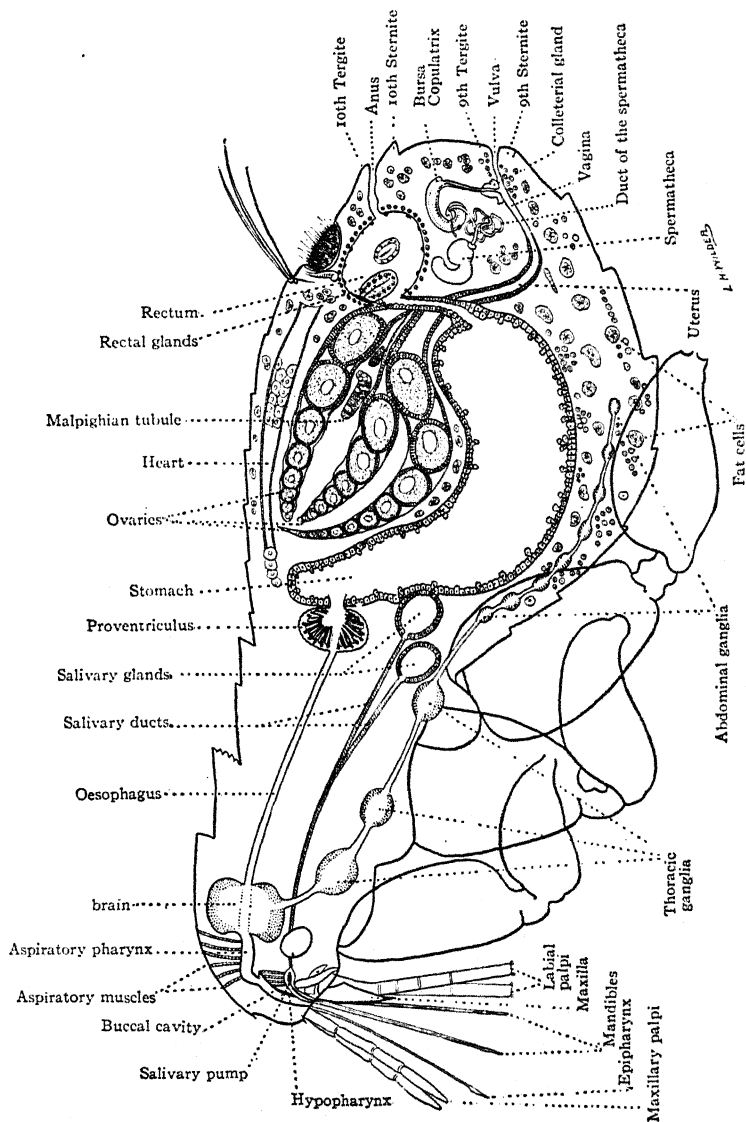


FIG. 194. Internal anatomy of a ♀ flea. (After Carroll Fox, *Insects and Disease of Man*, Blakiston.)

observed to jump 13 in. horizontally and as much as $7\frac{3}{4}$ in. vertically; equivalent jumps for a man of average height would be a broad jump of 450 ft. and a high jump of 275 ft. All the legs are furnished with rows of stout spines and are armed at the tip with a pair of large claws.

Simple eyes are present in some species of fleas but not in others. The antennae are short and club-shaped and consist of three segments,

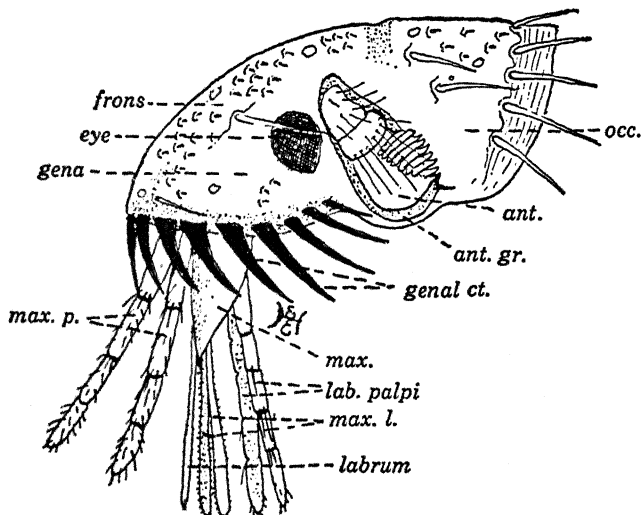


FIG. 195. Head and mouth parts of a flea, *Ctenocephalides felis* ♀; ant., antenna; ant. gr., antennal groove; genal ct., genal ctenidium; lab. palpi, labial palpi; max. l., maxillary laciniae or stylets; max., maxillary plate; max. p., maxillary palpi; occ., occiput. (In Fig. 194 the labrum is erroneously labeled "epipharynx," and the maxillary laciniae, "mandibles.") (Adapted from Ewing and Fox, U. S. Dept. Agric. Misc. Publ. 500, 1943.)

two small, the third large and laminated. When not in use they are folded back into special grooves for them on the sides of the head (Fig. 195, ant. gr.), but they can be rotated out or up over the head like a pair of horns. In many fleas there is a frontal notch or tubercle on the front of the head. The region behind the antennal groove is called the occiput; the region in front of it is more or less divided into a forward frons and a lower gena (see Fig. 195).

The mouth parts (Fig. 195) are fitted for piercing and sucking. The labial palpi, usually with three to five segments, are elongated, grooved structures that fit together to form a sheath for the piercing organs. These consist of a pair of slender maxillary stylets (laciniae), which are serrated at the tip like little saws, and a bristle-like epipharynx grooved on its posterior surface to form a food channel in conjunction with the maxillary stylets. The stylets also form a canal that

serves as a salivary duct. The basal parts of the maxillae (maxillary plates) are large pyramidal structures with a spine at the tip, used to hold the flea in position while feeding; they are provided with large four-segmented maxillary palpi which might be mistaken for antennae.

Male fleas are easily distinguished by the rakish upward tilt of the abdomen, which in females is rounded (Figs. 193, 194). The terminal segments are modified into complicated claspers for holding the female, and a remarkable intromittent organ which is so complex that one morphologist concluded that "truly, the thing does not make sense." The claspers have a broad immovable lobe or process and a movable *finger*. The details of these genital organs are of great taxonomic value, but difficult to use unless there are illustrations to go by (Fig. 196). In the females the terminal segments of the abdomen are reduced and inconspicuous. In this sex a taxonomic character of great importance is the form of the spermatheca (Figs. 194, 201), which is chitinized and easily seen inside the abdomen in cleared specimens.

Classification. Over a thousand species of fleas have been described. The differentiating characters are sometimes so subtle that only an experienced siphonapterologist can do the job, and then perhaps only if he has a particular sex under his microscope. Also, importance attached to taxonomic characters change. Major groups were once based on whether or not the head was "broken" dorsally between the antennae, and on the "telescoping" of the thorax. In the latest and well-received classification of Jordan (in Smart's *Insects of Medical Importance*, 1948) these characters are reduced to subfamily value, and fleas with narrow thorax fall into two different families (*Tunga* in Tungidae and *Echidnophaga* in Pulicidae).

Jordan divided the fleas into two superfamilies, Pulicoidea and Ceratophylloidea, based not on any single character but on a combination of them, of which perhaps the most reliable for identifying the Pulicoidea are (1) the presence of a vertical ridge on the outer wall of the midcoxa, (2) metepimeron extending far upward with its spiracle well out of line with the other abdominal spiracles, and (3) at most one row of bristles on the abdominal segments. The Pulicoidea contain the families Tungidae and Pulicidae; the former contains the genus *Tunga* (chiggers) and the latter the majority of the important annoying and disease-carrying fleas—*Pulex*, *Echidnophaga*, *Ctenocephalides*, and *Xenopsylla*. The Tungidae have a "telescoped" thorax, a pygidium with only 8 pits on each side, and no antepygidial bristles, whereas the Pulicidae have broad thoracic segments (except *Echidnophaga*), 14 pits on each side of the pygidium, and 1 or more antepygidial bristles.

The Ceratophylloidea are divided into 15 families, but only 3 of these contain species that are important to man or his domestic animals: Ceratophyllidae (see below), Leptopsyllidae, and Ctenophthalmidae. Each of the last two contains one important rat and mouse flea, *Leptopsylla segnis* and *Ctenophthalmus argyrtus*, respectively.

The following is a purely artificial key to the common fleas in or around human habitations, or important as vectors of plague or typhus:

- 1a. No ctenidia 2.
- 1b. At least one ctenidium present 5.
- 2a. Dorsal plates of thorax very narrow, appearing telescoped 3.
- 2b. Metanotum as long as or longer than 1st abdominal tergite 4.
- 3a. Pygidium with only 8 pits on each side; inner side of hind coxa without spine-like bristles; no antepygial bristles; female with abdominal spiracles II-IV very small or absent, V-VII very large *Tunga*.
Important species: *T. penetrans*, the chigger.
- 3b. Pygidium with 14 pits on each side; inner side of hind coxa with spine-like bristles; 1 or more antepygial bristles present *Echidnophaga*.
Important species: *E. gallinaeum*, sticktight flea of poultry, rats, etc.
- 4a. Mesothorax without a vertical rod; frons smoothly rounded *Pulex*.
Important species: *P. irritans*, human flea.
- 4b. Mesothorax with a vertical rod; suture between antennal grooves feebly chitinated *Xenopsylla*.
Important species: *X. cheopis* (most important plague and typhus vector), *astia*, *braziliensis*, *philoxera*, *hawaiiensis*.
- 5a. Genal and pronotal ctenidia present 6.
- 5b. Only pronotal ctenidium present 7.
- 6a. Genal ctenidium horizontal, in the common species on cats and dogs with 8 or 9 teeth on each side *Ctenocephalides*.
Important species: *C. canis* and *C. felis*, cat and dog fleas.
- 6b. Genal ctenidium of 3 spines with a broad genal lobe above and posterior to the spines *Ctenophthalmus*.
Important species: *C. argyrtus* of rats and mice in Europe.
- 6c. Genal ctenidium vertical, with 4 spines *Leptopsylla*.
Important species: *L. segnis* of rats and mice.
- 7a. One row of bristles on each abdominal segment *Hoplopsyllus*.
- 7b. Two rows of bristles on each abdominal segment, metanotum with short apical spines *Ceratophyllidae* (= *Dolichopsyllidae*).
18 genera, mostly on rodents and birds; for important genera and species, see paragraph below.

The family Ceratophyllidae constitutes what was the single genus *Ceratophyllus* until 1933 but which is now split into about 20 genera. Most of these are parasites of rodents or rabbits, but the genus *Ceratophyllus* (in the strict sense) contains parasites of birds; two of these, *C. gallinae* in Europe and eastern United States and *C. niger* in western United States, are pests of poultry. They are distinguished by having 24 or more spines in the pronotal comb. Many of the rodent genera

are fairly limited to particular kinds of rodent hosts; others show little specificity. *Nosopsyllus fasciatus* (Fig. 197C) is the commonest flea of domestic rats in temperate climates. It has 18 or 20 teeth in the pronotal comb. Some of the more important potential transmitters of sylvatic plague in this family in the United States are *Diamanus montaus*, *Oropsylla rupestris*, *Thrassis* spp., and *Opisocrostis bruneri* and *O. tuberculatus* of ground squirrels; *Orchopaeus sexdentatus* of wood rats; species of *Oropsylla* and *Thrassis* on marmots; and *Opisocrostis hirsutus* and *O. labis* on prairie dogs. Identification of the genera and species in this family is beyond the scope of this book, and students are referred to Ewing and Fox (1943) and Hubbard (1947).

Habits. Most fleas are neither as strictly host parasites as lice nor as strictly nest parasites as bedbugs. The nests or lairs of the host are the normal breeding places and are the homes of the eggs, larvae, and pupae; frequently adults are found in them too, but these are often either newly emerged fleas or fleas which have dropped off to deposit eggs. Many rodent and bird fleas are more frequently found in the nests than on the bodies of the hosts; Wayson (1947) found over 1000 fleas in each of 13 rodent nests in an area where the average number on each of 500 trapped animals was 3. In Russia fleas were found to move in and out of the burrows of ground squirrels at night. Some species, as already noted, seem to leave their hosts to deposit their eggs in the dens or lairs, whereas others lay the eggs at random in the fur of the host, whence they drop off when the animal shakes himself or prepares to sleep.

It is significant that mammals which have no permanent habitations, such as monkeys and deer, are nearly free of fleas, although they seldom lack lice. The human flea drops its eggs in the dust and debris in cracks in floors, under carpets, etc. Fleas seldom remain long on the body of a dead host.

Flea larvae thrive on blood, and some, e.g., *Nosopsyllus fasciatus*, are said to require it, yet they have no means of their own for obtaining it and the parents have to provide it in a semidigested condition in their feces. It is evident that the tendency of some fleas to leave their hosts for egg laying mainly in the nests is a wise provision of nature for the satisfactory nourishment of the larvae. Possibly the warmth generated by the host in its nest while sleeping or some odors connected with it indicate to the flea that the time and place are right for an excursion off the host.

Although most fleas show some degree of preference for particular hosts with which they are normally found associated, many species are not nearly so closely limited as lice are and may be found on a wide

variety of hosts. When hungry they suck blood wherever they can find it, and it is because of this that some rodent fleas are of importance to man as transmitters of such rodent diseases as plague and endemic typhus. Some species of rodent fleas, however, require less provocation than others to suck human blood.

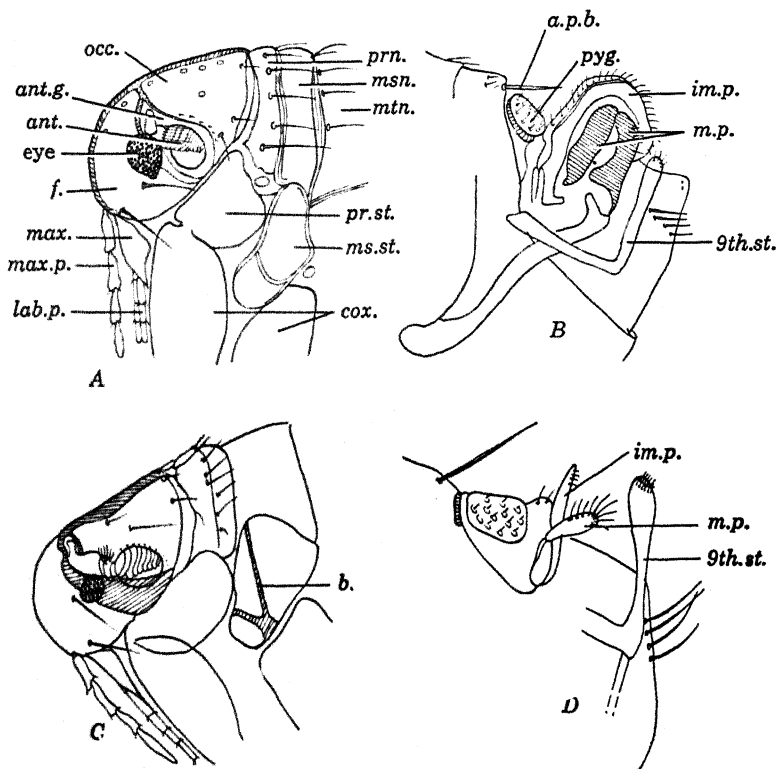


FIG. 196. A and B, head of posterior end of ♂ of *Pulex irritans*; C and D, same of *Xenopsylla cheopis*; ant., antenna; ant.g., antennal groove; a.p.g., antepygidial bristle; b, chitinized bar of mesosternum of *Xenopsylla*; cox., coxae; f., frons; im.p., immovable process of clasper; lab.p., labial palpi; max., maxilla; max.p., maxillary palpi; m.p., movable process of clasper (double in *Pulex*); msn., mesonotum; ms.st., mesosternum; mtn., metanotum; occ., occiput; prn., pronotum; pr.st., prosternum; pyg., pygidium; 9th st., 9th sternite. (Adapted from Fox, *Fleas of Eastern United States*, Iowa State College Press.)

The fleas found in human houses are mainly of three types: (1) human fleas (*Pulex*) (Fig. 196); (2) cat and dog fleas (*Ctenocephalides*) (Fig. 197A); and (3) rat and mouse fleas. The last vary in kind in different parts of the world; in warm climates and in sea-ports elsewhere they are species of the genus *Xenopsylla* (Figs. 193,

196), the foremost transmitters of plague, but in temperate climates they are mainly *Nosopsyllus fasciatus* (Fig. 197C) on rats, and *Leptopsylla segnis* (Fig. 197B) on rats and mice. In southern United States *X. cheopis* is most prevalent in summer, *L. segnis* in winter and spring. *Echidnophaga gallinacea*, the sticktight flea (Fig. 201), is also common on rats at all seasons.

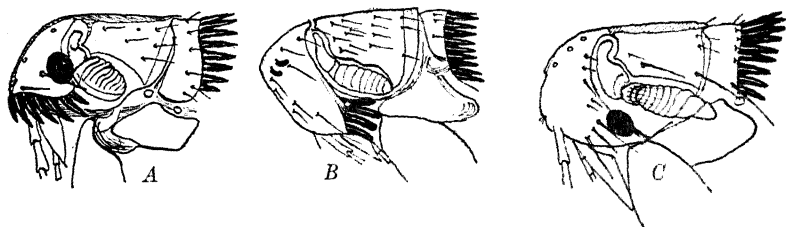


FIG. 197. Heads of fleas, showing arrangement of ctenidia. A, *Ctenocephalides canis*; B, *Leptopsylla segnis*; C, *Nosopsyllus fasciatus*. (After Carroll Fox, *Insects and Disease of Man*, Blakiston.)

Life Cycle. The eggs of fleas are oval, pearly-white objects of relatively large size, sometimes one-third the length of the parent flea. Except for the chiggers they are laid several at a time, the total number laid by one female being 300 to 400. The eggs hatch in from 2 to 3 days to over 2 weeks, depending on temperature. Eggs of *N. fasciatus* will hatch at temperatures as low as 41°F., but those of *Pulex* and *Xenopsylla cheopis* require higher temperatures. The most favor-



FIG. 198. Developmental stages of fleas. Left, larva of *Xenopsylla cheopis*. (After Bacot and Ridewood, *Parasitology*, 7, 1914.) Right, dust-covered cocoon of *Pulex irritans*. $\times 12$.

able conditions for the development of most species are temperatures between 65° and 80° and a humidity of 70 per cent or more. The higher the temperature the greater the humidity required. In the nests and holes where fleas breed, however, the "microclimate" may be favorable even when conditions in the open are highly unfavorable.

The larvae (Fig. 198) are tiny cylindrical maggot-like creatures with neither legs nor eyes. They have small brown heads and whitish bodies composed of 13 visible segments and a hidden terminal one, all

provided with rather sparse bristly hairs to aid in crawling. The last segment is terminated by a pair of tiny hooks.

The larvae avoid light and feed upon what bits of organic matter they can find, such as mouse "pills," crumbs, hairs, epidermal scales from their hosts, and the excrement of adult fleas. The larvae can be reared successfully in the laboratory when favorable temperature and humidity are constantly maintained and when they are fed on dried blood, fragments of dog biscuits, mouse "pills," etc. Some species, if not all, devour their shed skins after molting. *X. cheopis* can develop to the adult stage on flour alone, which might enable it to survive prolonged transport in grain even without rats. The duration of the larval stage varies with climatic conditions and food and to some extent also with the species. Some species may pass through their two molts and enter the pupal stage in a week, whereas under unfavorable conditions the larval existence may be drawn out to over 3 months.

When ready to undergo their transformation into adults, the larvae spin little silken cocoons that are somewhat viscid, so that particles of dust, lint, or sand readily adhere to them (Fig. 198). Under favorable conditions it usually takes from 1 or 2 weeks to a month before the adults emerge from the cocoons, but at low temperatures or in dry weather the insects may remain dormant in their cocoons for several months and thus tide over unfavorable seasons such as northern winters or dry seasons in the tropics. The complete life cycle takes a minimum of 3 weeks in the tropics and from 4 to 6 weeks in temperate climates.

The adult fleas do not become sexually mature or copulate for some days after they escape from the cocoon. Soon after copulation egg laying begins but no breeding takes place without blood meals.

The length of life of adult fleas depends largely on food supply, temperature, and humidity. At low temperatures (60°F.) well-fed fleas will live for at least 18 months. In the absence of a host they have less endurance than ticks or even bugs, but *Pulex* sometimes survives for 3 or 4 months under ordinary conditions and for a year or more at low temperatures. *X. cheopis* may survive for a month. Dog fleas certainly survive for several weeks, and rodent fleas survive for at least 4 months in the nests of hibernating ground squirrels. The optimum climatic conditions and normal length of life probably vary a great deal with different species. Most of the *Ceratophyllus* group and also *Pulex irritans* are fleas of temperate or cold climates, while the species of *Xenopsylla* are characteristic of hot climates.

Unlike most bloodsucking insects, fleas usually feed at frequent intervals, generally at least once a day and sometimes oftener. Fleas frequently feed even when the digestive tract is already well filled, and

may pass practically unaltered blood in their feces to be utilized, second-hand, by the larvae.

Fleas and Disease

Like most other bloodsucking parasites, fleas are intimately connected with the transmission of disease. The most serious charge against them is the dissemination of bubonic plague, which alone is sufficient to rank them among the most important insect enemies of man. Fleas are also the usual transmitters of the endemic or murine form of typhus; they are important transmitters of tularemia among rodents; they serve as intermediate hosts of certain tapeworms; and they have been suspected in connection with other diseases.

FLEAS AND PLAGUE

Plague, although primarily a disease of rats and other rodents, ranks as a human scourge with such diseases as smallpox and leprosy. It is estimated that in the epidemic of the fourteenth century in Europe one-fourth of the population of that continent, or 25 million people, died of the disease, and superstition and unreasoning terror led to horrible persecution and torture. At present the disease is largely confined to tropical countries and is especially prevalent in India, where an average of over half a million deaths a year are caused by it.

With our new methods of control, however, Meyer (1947) thinks it unlikely that urban plague will henceforth be a major problem except in a few blighted areas. In the past it was often introduced from the tropics into other countries. In temperate climates it does not usually become epidemic but establishes itself in the local rat population where it may smolder on for a long time in an endemic condition, causing sporadic human cases which may be secondarily followed by local outbreaks of the pneumonic form of the disease. In some countries the disease has become secondarily established in wild rodents (called sylvatic plague) and may then remain indefinitely.

Plague, caused by a small bacillus, *Pasteurella pestis* (see p. 234), exists in man in bubonic, septicemic, and pneumonic form. The bubonic form results from infection through the skin, usually by the bite of an infected and "blocked" flea (see below). After a short incubation period there is a sudden high fever, mental disturbance, and severe prostration, with characteristic large swollen lymph glands called buboes. The septicemic form is characterized by invasion of the general blood stream, and the pneumonic form by rapid multiplication of the bacilli in the lungs. The latter usually follows direct passage of the disease from man to man via the respiratory tract. There

is some hope of recovery from bubonic plague, but the other forms are almost always rapidly fatal if untreated. Two pneumonic outbreaks in California caused the death of 13 of 14 and 30 of 32 cases, respectively, in 1919 and 1924, before antibiotics were available for treatment.

Mechanism of Transmission. With few exceptions the great epidemics of plague follow epizootics among house rats. As these animals succumb to the disease their orphaned fleas attack man and convey the infection to him. The usual mechanism of transmission was made

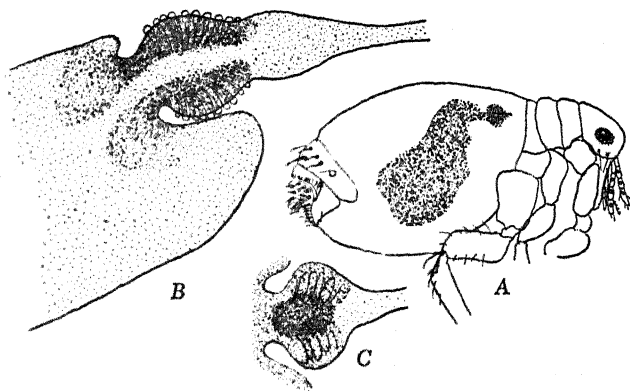


FIG. 199. Blocking of fleas by plague bacilli. *A*, position of proventriculus and stomach of flea as they appear when full of blood. *B*, proventriculus and fore part of stomach partially blocked (heavily shaded area). *C*, proventriculus completely blocked. (*B* and *C* adapted from Esky and Haas, *Publ. Health Bull.* 254, 1940.)

clear by the work of Bacot and Martin in 1914. They observed that the Indian rat flea, *Xenopsylla cheopis*, after feeding on an infected animal, often had its digestive tract completely blocked by solid growths of plague organisms (Fig. 199). Such "blocked" fleas are unable to ingest more blood and in attempting to do so they regurgitate plague germs into their victims.

Fleas do not remain infective indefinitely; in hot weather they usually lose their infection in a week, though in cool weather it may last for 15 days. Many of them die as a result of the infection, especially in hot, dry weather, since they are unable to overcome the effects of desiccation by imbibing fresh blood. Since the infected fleas live such a short time in warm climates, epizootics subside quickly, and with them the human epidemics. The bites of fleas that do not become blocked are never infective, although the feces are. The feces may remain infective in dark, damp places for over a year and cause infections in rodent burrows long after the fleas have gone. This also

might account for the continued occurrence of human cases after a rat epizootic has died out, for human or dog fleas might infect bites with their feces even if not blocked. Such a situation was reported by Rotman in 1945 in Dakar, where DDT dusting of human clothing was resorted to.

Tropical Epidemic Plague. The species of *Xenopsylla* are the only fleas of domestic rats in which *Pasteurella pestis* thrives well enough to cause blockage regularly, and it is for this reason that human plague epidemics are almost universally associated with these fleas and quickly die out in their absence. Even all the different species of *Xenopsylla* are not equivalent. *X. cheopis* is more readily blocked, and under a greater range of climatic conditions than others of its genus. It is further qualified as a plague vector by the fact that it needs less provocation to feed on man than do most rodent fleas. *X. braziliensis* is an almost equally good transmitter in parts of Africa where it is abundant. *X. astia*, on the other hand, which is widely distributed along with *cheopis* in India and Ceylon, is a much poorer vector and functions only under special climatic conditions.

Imported Plague Epidemics. Plague is dispersed from one part of the world to another either by transportation of infected rats with their *Xenopsylla* on ships or railway cars or by the transportation of the fleas alone, for example, in grain in which rats were formerly present. However, in view of the short time in which infected fleas either lose their infection or die, such fleas would not be likely to start an epidemic after more than two weeks apart from their hosts. Although in the past plague has been repeatedly introduced into the northern cities of America and Europe, it has never succeeded in becoming permanently established, and epidemics soon die out, although the epizootics sometimes continue to smolder for a long while. In these places *Nosopsyllus fasciatus* and to a lesser extent *Leptopsylla segnis* and *Ctenophthalmus argyrites* largely replace *Xenopsylla* on rats. These fleas rarely become blocked and so fail to transmit the infection by their bites. *X. cheopis* is permanently established and is the dominant flea on rats in seaports in all warm parts of the world. It has also established itself in inland cities in southern United States and even in places like Denver, St. Louis, and Washington, but here it is largely confined to a few premises or a part of a city, where it is protected in winter. Even in the southern states it almost dies out in cold weather.

Sylvatic Plague. This form of the disease results from the spread of the infection from domestic city rats—mostly Norway rats and roof rats—to wild rodents on the edges of the cities or in suburban areas, where a certain amount of interchange of fleas takes place. Plague is

believed to have been introduced into San Francisco in 1900, whence it spread to ground squirrels in the surrounding counties and eventually all over western United States, now having reached east to West Texas, Kansas, and the Dakotas. In 1920 it entered ports on the Gulf Coast of Texas, but died out without establishing itself in sylvatic form.

Most if not all species of rodents, and many other animals, are susceptible to plague, and often die of it; but certain kinds, because of their gregarious habits or relation to man, are more important than others as reservoirs of sylvatic plague. These are particularly ground squirrels (*Citellus* spp.), prairie dogs (*Cynomys* spp.), pack rats (*Neotoma* spp.), and marmots (*Marmota* spp.), and to a less extent various species of mice or voles. In most parts of the United States ground squirrels are of preeminent importance as reservoir hosts. Prairie dogs have a more discontinuous distribution; whole "towns" of them may be wiped out. Ranchers aid in distribution of plague by capturing sick animals and setting them free on their own ranches many miles away, to transmit their infections to new colonies and thus exterminate them. This reminds me of a friend who unwittingly kept a black widow spider as a pet in her house because it killed flies and mosquitoes. One enterprising boy in Colorado was found catching sick prairie dogs and selling them to unsuspecting tourists as souvenirs!

In the United States plague infection has been found in some 40 species of wild rodents, and about 35 species of fleas have been found plague infected in nature or experimentally; some of the more important ones were mentioned on p. 625. The importance of particular species varies, depending on how easily and quickly they become infected, how long they remain infected, how readily they become blocked, and how long they live after becoming infective. Of the fleas on wild rodents in the United States, *Diamanus montanus* is one of the best vectors. Human cases may result from bites of blocked fleas, but in its sylvatic form more often from handling infected rodents; the rodents may be infected by blocked fleas, by biting or eating infected fleas, by scratching fleas or their feces into their bites, or by cannibalism. Blocked fleas bite much more frequently and persistently than normal fleas.

Human cases of sylvatic plague are remarkably rare; there have been only about 67 isolated cases and two pneumonic outbreaks traced to wild rodents in the United States since 1900, and in some states no human cases have been reported, even when fields and canyons are littered with carcasses of plague-killed rodents.

There is some danger that as an epizootic encroaches on a city the infection may reverse its procedure and jump back from wild rodents

to domestic rats. Such an occurrence probably accounts for San Francisco's second city-wide outbreak in 1907-1908, four years after her first one died out. The danger is greatest in cities having rats infested with *X. cheopis*, surrounded by areas inhabited by ground squirrels. Having sylvatic plague in your suburbs is like having a rattlesnake on your golf course or a Typhoid Mary in your kitchen. It is an unpleasant threat.

Other important foci of sylvatic plague exist in central Asia and southeast Russia, where *Citellophilus tesquorum* is the chief vector among ground squirrels and marmots; in Manchuria, where *Oropsylla silantiewi* transmits among marmots and where in 1910-1911 an outbreak with 60,000 victims occurred among people hunting marmots for their skins; in South Africa, where *Xenopsylla philoxera* transmits it among wild gerbils and to the semidomestic multimammate mouse, *Mastomys coucha*, which comes into houses and passes on the disease to domestic rats which harbor *X. braziliensis*; and in the Argentine pampas, where a species of *Rhopalopsyllus* (one of the few combless fleas in the Dolichopsyllidae) transmits among small rodents (*Graomys*) and hares.

Sylvatic plague is comparable to typhus, relapsing fever, and yellow fever, all of which smolder silently and often unnoticed in their reservoir hosts, only flaring into epidemics when they come in contact with vectors that are closely associated with human beings and habitually or frequently bite them.

Control of plague will be considered along with that of endemic typhus, another disease transmitted from rodents to man by fleas, on p. 640.

FLEAS AND TYPHUS

In 1926 Maxcy pointed out that the epidemiology of sporadic cases of typhus occurring in southern United States was not suggestive of louse transmission but had the earmarks of a disease transmitted only occasionally to man from a rodent reservoir. Subsequent work by Dyer and his colleagues of the U. S. Public Health Service showed that this was true and that this endemic type of typhus (see p. 229) existed among rats and was transmitted principally by fleas. The disease is associated with rat-infested localities such as granaries, markets, and restaurants and is now known to occur in practically all temperate and tropical regions of the world. A number of species of fleas, including the sticktight (*Echidnophaga gallinacea*), various rodent fleas, and the cat and dog fleas (*Ctenocephalides*), become infected and are potential transmitters, but *Xenopsylla cheopis* is undoubtedly most important as

a transmitter to man. In the southern States the curve of human typhus closely corresponds to the seasonal curve of abundance of *X. cheopis* (Figs. 193, 196). Fleas, unlike lice, are not harmed by typhus infection and may remain infected for life and for some time after death, but they do not transmit the infection to their offspring. After initial infection from a rodent flea, the infection may be spread from person to person by lice (see p. 608).

The disease in man is much milder than the epidemic louse-borne type and also differs from it in causing scrotal swellings in guinea pigs. In rats and mice it is usually symptomless; since the rats do not die from it their fleas are not forced by hunger to seek human blood. Besides, there is no mechanism like the blocking in plague to enable the fleas to transmit the disease by their bites; only their feces and crushed bodies are infective. Since this is much less likely to lead to human infection than the mechanism involved in epidemic plague transmission, human cases of this disease are sporadic, like sylvatic plague. Some cases may result from contamination of food by urine of infected rats or from handling the rats themselves. Endemic typhus exists in wild rodents and other small mammals as well as in house rats.

In the United States typhus is endemic principally in the southern states. Up to 1930 few cases were reported but after that time the disease became commoner year by year at an accelerating rate, until in 1945 over 5000 cases were reported, the largest numbers being in Texas and Georgia. In a survey in one Texas county 94 per cent of urban and 80 per cent of rural buildings harbored rats which by blood test were positive for typhus; and of 213 pools of the three commonest rat fleas (*Xenopsylla cheopis*, *Nosopsyllus fasciatus*, and *Leptopsylla segnis*), 53 harbored typhus. Some of these were found on kittens, puppies, and opossums.

The disease has repeatedly been introduced to more northern cities such as Washington, Cincinnati, and St. Louis along with *X. cheopis* which were presumably left behind in freight cars or trucks by frightened rats. In such places, however, *X. cheopis* remains very localized or fails to establish itself permanently. Otherwise the gradual encroachment of this infection from the south and of plague from the west would be an unpleasant outlook for midwestern cities. Since 1945 the number of typhus cases has steadily decreased until in 1952 and 1953 there were only a few over 200 cases each year, a 96 per cent reduction. This is due to a vigorous anti-typhus campaign by the Public Health Service and the individual states through DDT dusting of rat runs (see p. 641), poisoning of rats with "1080" (fluoroacetate), warfarin, and other raticides, and ratproofing of buildings.

FLEAS AND OTHER DISEASES

Fleas easily become infected with tularemia (see p. 574), and may remain carriers for a month, but they are probably not important transmitters. They also transmit Whitmore's bacillus, causing a glanders-like disease in rodents and man in southeastern Asia. Tovar in 1947 reported that fleas, as well as bedbugs and ticks, could transmit undulant fever or brucellosis (see p. 575). Fleas serve as intermediate hosts for the non-pathogenic rat trypanosome, *Trypanosoma lewisi*, and quite possibly for the related trypanosomes of other rodents also. *T. cruzi*, however, although it develops in such different arthropods as ticks and bugs, undergoes rapid degeneration in fleas. This is also true of relapsing-fever spirochetes. Fleas were long suspected of transmitting infantile and canine leishmaniasis (see p. 137) in the Mediterranean region. The occurrence of a natural *Leptomonas* in fleas provided considerable circumstantial evidence against them, but they were finally acquitted.

Fleas serve as intermediate hosts for certain tapeworms, among them *Dipylidium caninum* (see p. 366) of dogs and cats, which is occasional in children, and *Hymenolepis diminuta* and *H. nana* of rats, mice, and man (see pp. 363 and 364). The eggs are ingested by larvae, but the cysticercoids finish their development in the adult fleas.

Notes on Important Species of Fleas

Human Flea. The only species of flea that is known to be a parasite of man primarily, with the exception of the chigger, is the appropriately named *Pulex irritans* (Fig. 196A, B), though in many places man is annoyed more by certain other species that are primarily parasites of his domestic animals. This flea is also a pest of pigs, and it has been found on dogs and other carnivores, on deer, and occasionally on rats and mice. It probably originated in Europe, whence it has been introduced to all parts of the world, but is relatively rare in the tropics. This flea is the species that has made California as famous for its fleas as New Jersey is for its mosquitoes. A cool, humid summer climate combined with a mild, wet winter is ideal for this pest.

The susceptibility of different individuals to flea bites is variable. Some people are apparently entirely immune to flea bites and feel no pain from them. The writer on his first visit to California, warned to expect trouble from fleas, was pleasantly surprised to feel no discomfort other than tickling as the fleas promenaded, while a roommate spent many sleepless hours in pursuit of the wily fleas and in violent massaging of painful wounds. According to work by McIvor and

Cherney immunity can be artificially induced in most people by injection of antigens made from pulverized fleas (see p. 512). The human flea is not an important plague transmitter because it seldom becomes "blocked," but it may cause some infections by its feces.

Dog and Cat Fleas. Next in frequency to the human flea as parasites of man are the dog and cat fleas, *Ctenocephalides canis* and *C. felis*. In the southeastern United States where the flea scourge competes very well with that of California, these are the species usually met with. During the moist, hot summers they become exceedingly abundant. Although primarily parasites of dogs and cats they willingly include man in their bill of fare when the preferred hosts are not readily available. A case once came to the writer's attention in which the residents of a house were unmercifully bitten after disposing of a badly infested dog and two or three cats, although there had previously been no annoyance. Cat and dog fleas readily go from one of these hosts to the other. These fleas can easily be distinguished from any other common species by the presence of *two* well-developed ctenidia (Fig. 197A), each with numerous teeth.

The eggs are usually laid loosely in the fur, whence they fall out when the host shakes himself or is settling himself for a nap. They develop in the dust and dirt of kennels, woodsheds, house floors, or other places where infested animals are likely to go. Patton and Cragg found the inside of a hat in which a kitten had slept overnight so full of flea eggs that it looked as if it had had sugar sprinkled in it.

Dog and cat fleas, from their habits, are the species most frequently implicated in the transmission of the dog tapeworm (*Dipylidium*) to children. These species are even less frequently concerned with plague transmission than is *Pulex irritans*.

Rodent Fleas. The various species of fleas that infest rats, ground squirrels, and sometimes other rodents are only accidental parasites of man. If it were not for their importance in the spread of plague and typhus they would need no special consideration. For identification of the commoner species refer to the key on p. 624.

The combless fleas of the genus *Xenopsylla* (Fig. 193), which are of the greatest importance in transmission of epidemic plague among domestic rats and man, and of murine typhus to man, are primarily residents of Asia and Africa. *X. cheopis*, however, probably originally from the upper Nile valley, has accompanied rats to all important seaports in the world and thence inland in many places (see p. 631). This species attacks man more readily than most rodent fleas when deprived of its normal hosts.

There are a number of other species of *Xenopsylla* on rats (see p.

631). *Xenopsylla cheopis* and *X. astia* are readily distinguished by the form of the spermatheca in females (Fig. 200) and by the ninth abdominal sternite in the males. *X. brasiliensis* is the prevalent rat flea in central Africa, but it also occurs irregularly in hot parts of India, Brazil, and other tropical countries. *X. philoxera* (= *eridos*) is a species found on veldt rodents in South Africa and is associated with endemic plague there. *X. hawaiiensis* is common on field rats in Hawaii but not on house rats.

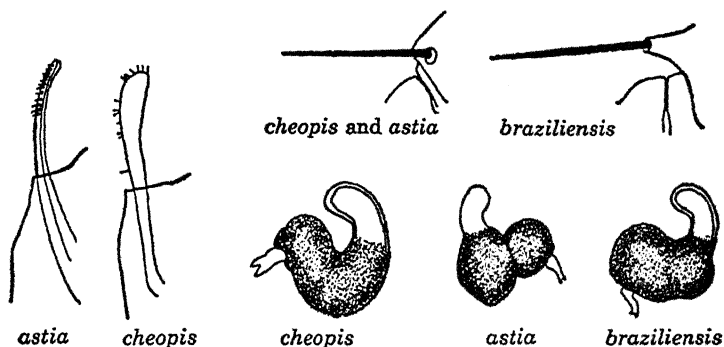


FIG. 200. Differential characters between common species of *Xenopsylla*. Left, 9th sternites; top right, antepygial bristles; lower right, spermathecae. (From *Trop. Diseases Bull.*, 20, 1923.)

In temperate climates the genus *Xenopsylla* is largely replaced on rodents by fleas of the family Ceratophyllidae and a few others (see p. 631). The Ceratophyllidae are characterized by having a well-developed pronotal comb only, and two rows of bristles on each abdominal segment.

Nosopsyllus fasciatus (Fig. 197C) is the most prevalent flea on domestic rats in temperate climates, and *Leptopsylla segnis* (Fig. 197B) is also very common on rats and mice in many places; it ranks next to *X. cheopis* in southern United States. All three of the commonest rat fleas, as well as the domestic rats (*Rattus* spp.) and the house mouse are, like some of our other worst pests (e.g., *Aedes aegypti* and *Musca domestica*), imported from the Old World. The most important of the many fleas found on wild rodents in North America are mentioned in the key on pp. 624 and 625. The sticktight flea (see following section) is also often found on rats and is a plague carrier.

Bird Fleas. There are three important fleas of poultry. One, the small sticktight flea, *Echidnophaga gallinacea* (Fig. 201), belonging to the family Pulicidae (see p. 623), has a world-wide distribution in warm countries, and is the most important flea pest of poultry in the United

States. This flea sticks tight to its host in one place; it is gregarious, collecting in clusters on the heads of poultry, in the ears of mammals, etc. It burrows to some extent, causing considerable irritation. Besides poultry, it attacks dogs, cats, rabbits, rats, and other mammals and birds, and not infrequently children. The eggs are scattered on hen-house floors, dog yards, etc. Since this flea is susceptible to plague and attacks both birds and rodents, it may carry infection from wild to domestic rodents, and when attached to such birds as vultures, hawks, or pheasants may be a means of carrying it to distant places.

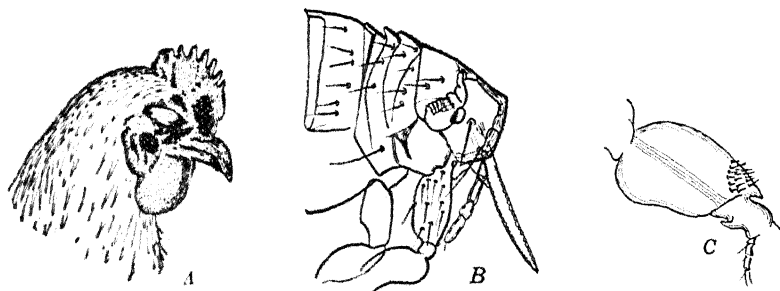


FIG. 201. *Echidnophaga gallinacea*, sticktight flea. A, clusters on head of a chicken; B, head of flea; C, inner aspect of hind coxa. (A, adapted from Bishopp; B and C from Fox, *Fleas of Eastern North America*.)

The other two important bird fleas are *Ceratophyllus gallinae* in Europe and eastern United States and *C. niger* in western United States. These have habits like those of rodent fleas, living primarily in the nests.

Chiggers. The chigger, jigger, or sand flea, *Tunga penetrans* (Fig. 202), is the pest which inspired the sailor's oath, "I'll be jiggered." Originally found in tropical America, it was introduced to west Africa with some ballast sand in 1872. It spread rapidly over nearly the whole of Africa but has failed to establish itself in Europe or India. The chigger is a small flea, only about 1 mm. in length, of the family Tungidae (see key, p. 623). The males and virgin females are similar to other fleas in habits, except that they attack a wider range of hosts. Man and pigs seem to be the principal hosts of this pest, but cats, dogs, and rats are also attacked.

The chigger breeds especially in regions with sandy soil shaded by heavy underbrush or in the earth floors of native houses. After emergence the fleas lie in waiting in debris on the ground and attack mainly the feet of animals or human beings which come their way. The particular importance of this flea lies in the fact that the impregnated females have the aggravating habit of becoming imbedded in the skin, especially in such tender spots as under the toenails. Here, nourished

by the blood of the host, the fleas produce eggs and retain them in the abdomen, causing it to swell into a great round ball as large as a pea. The head and legs appear as inconspicuous appendages (Fig. 202*B*). Only the two posterior segments of the abdomen do not enlarge; these project from the swollen inflamed skin to which the flea is embedded.

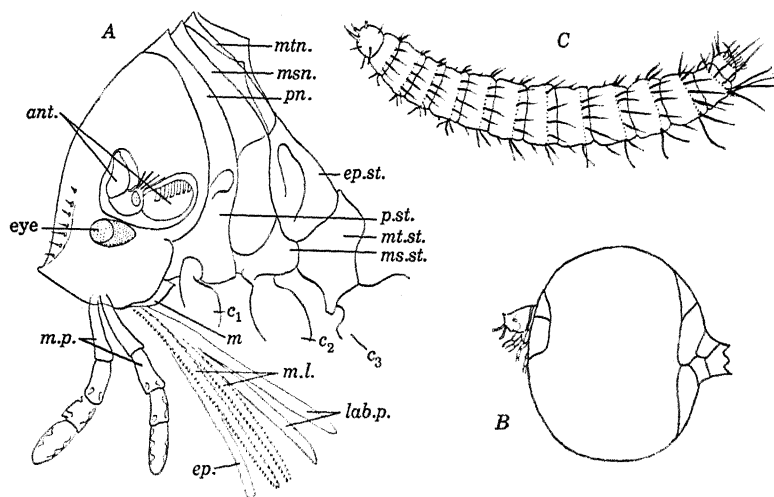


FIG. 202. *Tunga penetrans*, chigger. A, head and thorax (after Hubbard, *Fleas of Western North America*, 1947). B, gravid ♀ showing legs disintegrating (after Patton and Evans, *Insects, Ticks, Mites and Venomous Animals of Medical and Veterinary Importance, I, Medical*, Grubb). C, larva (after Faust and Maxwell, *Arch. Dermatol. Syphilol.*, 22, 1930). Abbreviations approximately as in Figs. 193 and 196A, except *m*, base of maxilla, and *m.l.*, maxillary laciniae.

The eggs, up to a hundred in number, mature in about a week and are then expelled by the female through the protruding end of the abdomen. Sometimes the entire gravid female is expelled.

The eggs fall to the ground, where they undergo development in the orthodox siphonapteran manner; the larvae (Fig. 202C) feed on organic debris, grow to maturity, pupate in a cocoon, and finally emerge as adults after 17 days or more. Faust and Maxwell, however, have observed an unusual case in which the thriving larvae were found in various stages of development in skin scrapings from the inguinal and pubic regions of a man who had been attacked in these parts by adult chiggers while sitting on some bales of sisal imported from Yucatan.

The wounds made by the burrowing female in the skin become much inflamed and very painful. Frequently the distended abdomen of a flea is crushed and the eggs released in the wound. In such cases the inflammation is greatly increased unless the crushed body and eggs

are immediately expelled. As soon as the eggs are laid, or even before, the skin surrounding the wound ulcerates and pus is formed. The empty female flea is expelled. The sore which is left is very liable to secondary infection, sometimes resulting in the loss of toes or even whole limbs through blood poisoning. In Central America deaths from tetanus and gas gangrene from chigger wounds are common.

Although usually only a few chiggers are present at a time, there are cases in which hundreds infest a person at once, literally honeycombing the skin and making the feet or other parts of the body so sore that the victim is rendered a complete invalid.

The treatment of chigger wounds formerly consisted in the destruction of the fleas while they were embedded in the wounds. This was done by applying insecticides or pricking with a needle, the dead insect being removed after ulceration. A better method is to enlarge the opening around the flea with a clean needle and remove the parasite entire, then carefully dress the wound and protect it until healed.

Houses, yards, etc., in chigger regions should be kept as free as possible of dust, dirt, and debris. In Central America Quiros recommended a prohibition against driving hogs affected with chiggers through the streets, along with regulations for treating affected hogs where they are raised. Spraying premises with a 2.5 per cent DDT suspension quickly eliminates chiggers. Dusting the feet and socks with DDT is the best means of personal protection.

Control of Fleas and Flea-Borne Diseases

Strict cleanliness in private homes or public buildings prevents fleas from breeding in them. Treatment with 5 per cent DDT in oil or emulsion (1 gallon per 1500 sq. ft.) or 10 per cent dust eliminates them from buildings and stops breeding in dog yards, kennels, etc., when applied to soil, rubbish, or floors. DDT dust rubbed into the fur of dogs (about 10 grams for a medium-sized dog) affords relief. Cats lick off the DDT and are sickened by it, but lightly dusting the sleeping places soon controls the situation.

Control of Plague and Endemic Tyhus. In controlling plague in the past reliance has been placed almost entirely on rat control, but this had its dangers, since the fleas, if not killed with the rats by fumigation with HCN, methyl bromide, or burning sulfur, were likely to turn their attention to man. This was especially true with typhus, since this disease does not kill the rats, and so only occasional human cases occur until the fleas are orphaned by poisoning, trapping, or driving off of their rat hosts. Often a rat campaign precipitates a number of human typhus cases.

Since the advent of DDT, it has become possible to control these

diseases without this danger from orphaned fleas. The procedure is first to dust harborage places and rat runs heavily with DDT or Chlordane and to blow it into the openings of burrows. Rats pick up enough DDT on their feet, tails, and fur to kill fleas not only on their own bodies but also in their nests. Depending on how thoroughly the dusting is done, the flea index on rats is reduced 80 to 99 per cent almost at once, and 75 to 80 per cent control can be expected after 4 to 6 months. In practice it takes about 2 to 3 lb. of 10 per cent dust per premise. Good control of fleas is also obtained by applying 5 per cent DDT emulsion to runways, harborage places, etc., in residences or other places where the dust is undesirable. Two or three days after dusting, rats may be destroyed by poisoning with some of the new rodenticides, such as Warfarin, "1080" (sodium fluoroacetate), or Antu. By these methods a half-dozen epidemics of plague have been suppressed in various parts of the world, including Peru, North Africa, Middle East, and Turkey. In Hyderabad a spectacular reduction in the amount of plague has been reported. The chief worry now is to what extent fleas, like flies, will become immune to DDT and allied chemicals. In local areas five species have already been reported to have developed resistance. In some situations fumigation with HCN to destroy both rats and fleas at once may be desirable. Additional protection, e.g., for military forces, is possible by the use of vaccines, which are available for both typhus and plague.

Both DDT dusting and rat poisoning are temporary measures. Permanent good comes only from ratproofing buildings where this is possible, as it is in American cities. The cost is low compared with loss from rats, even without considering their relation to disease, since rats usually outnumber the human population three to two, and the average cost of upkeep per rat for food and goods destroyed is estimated at one-half cent per day. That amounts to \$1.80 per rat per year, or a total of over \$250,000 for a city of 100,000 population.

If sylvatic plague outbreaks should occur near populated areas and there is danger of fleas transferring the disease to city rats, airplane dusting of the area would be worth a trial. Control of field rodents by poisoning or fumigation is slow, expensive, and discouraging.

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Diptera

I. Bloodsucking and Disease-Carrying Flies Other Than Mosquitoes

Importance. From a medical point of view the Diptera are as important as all other arthropods put together, for in this order are included the normal transmitters of malaria, trypanosomiasis, leishmaniasis, yellow fever, dengue, papatasi fever, Oroya fever, encephalomyelitis, and various types of filariasis. Without their dipteran transmitters these diseases would probably entirely disappear. Other diseases, such as anthrax, yaws, and pinkeye, are mechanically conveyed by flies, and the housefly and other non-biting flies are involved in the mechanical transmission of all kinds of filth diseases. Besides all this, the Diptera include nearly all the insects which infect wounds, skin, nasal passages, or digestive tract, in the larval (maggot) stage.

General Structure of Diptera. To understand the relations of these numerous important insects and their classification, we must make a brief survey of the characteristics and classification of the order Diptera. The whole order can usually be distinguished readily from other insects by the fact that there is only one pair of membranous wings, the second pair of wings being represented only by an insignificant pair of knobbed rod-like appendages known as halteres (see Fig. 225, *h*). Even in those forms in which the wings are secondarily absent the halteres are usually present. These are vibrated with great speed during flight (300 times per second) and act as balancers. In the Cyclorrhapha (houseflies, etc.) there is a membranous lobe at the base of the wing on the posterior side, called the *alula*; behind this, in many Cyclorrhapha are one or two additional lobes called squamae or calypteres (Fig. 245).

The legs consist of the usual segments (see p. 504), generally with long coxae. The tarsi are usually terminated by two claws with pad-

like "pulvilli" under them, and often a third appendage, the "empodium," between them, either bristle-like or resembling a third pulvillus. The head is joined to the thorax by a very slender, flexible neck. The thorax has its three component parts fused. The abdomen usually consists of four to nine visible segments and is terminated by the ovipositors or egg-laying organs in the female and by the claspings or copulatory organs in the male.

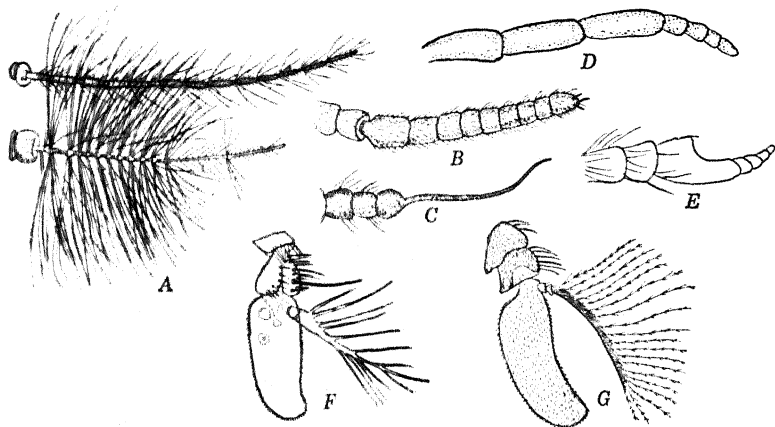


FIG. 203. Types of antennae of Diptera: A, ♀ and ♂ mosquito (*Culex*); B, *Simulium*, blackfly; C, *Chrysopila*, a lepid; D, *Chrysops dissimilis*; E, *Tabanus*; F, *Musca*, housefly; G, *Glossina*, tsetse fly.

The antennae and also the palpi are of considerable use in classification; the extent of the variations in the antennae may be gathered from Fig. 203. In the more generalized families, e.g., the Nematocera, the antennae consist of many segments which, except the basal two, are similar in form (Fig. 203A, B) and often bear whorls of hairs which in the males give a plumose effect, e.g., in male mosquitoes. In more specialized families the terminal segments tend to coalesce more or less (Fig. 203C, D, E), as in the tabanids and other Brachycera, or the segments beyond the third are reduced to a simple or plumose bristle or arista which appears as an appendage of the enlarged third segment (Fig. 203F, G), as in nearly all the Cyclorrhapha.

The mouth parts are profoundly modified in accordance with the habits of the flies. In the botflies, in which the adults live only long enough to reproduce their kind, the mouth parts and even the mouth are much degenerated; in the non-bloodsucking forms, such as the common housefly, the mouth parts are developed as a fleshy proboscis which is used for lapping up dissolved foods; in the bloodsuckers,

which are the forms that particularly interest us here, the mouth parts are developed into an efficient sucking and piercing apparatus. In the suborder Orthorrhapha (mosquitoes, sandflies, blackflies, and horseflies) the labium acts as a sheath for the other parts which are fitted for piercing and sucking; in the Cyclorrhapha (*Stomoxys*, hornfly, and the tsetse flies), the labium itself forms a piercing organ, and the epipharynx and hypopharynx form a sucking tube, the mandibles and maxillae being absent. The evolution of this type of proboscis is discussed and illustrated on p. 671.

Life Histories. All Diptera have a complete metamorphosis, but beyond that fact the life history varies within wide limits. Most flies lay eggs, some of which require several days of incubation; others

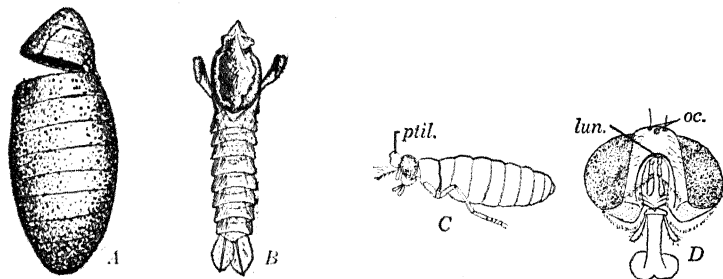


FIG. 204. *A* and *B*, types of pupal cases, showing manner of emergence of adults; *A*, empty puparium of blowfly, typical coarctate pupa of Cyclorrhapha; *B*, empty case of mosquito, typical obtected pupa of Orthorrhapha; *C*, newly emerged fly showing bladder-like ptilinum (*ptil.*) by which the end of the pupal case is pushed off; *D*, face of fly showing crescent-shaped scar of lunule (*lun.*) left by drying up of ptilinum; *oc.*, ocelli. (After Alcock, *Entomology for Medical Officers*, 1920.)

hatch within a few minutes. Others, e.g., the sheep nasal fly, *Oestrus ovis*, deposit newly hatched larvae, and still others, e.g., the tsetse flies and the Pupipara, do not deposit their offspring until they have undergone their whole larval development and are ready to pupate.

The larvae of Diptera may be simple maggots without distinct heads or appendages and capable of only limited squirming movements, e.g., the screwworms, or they may be active creatures with well-developed heads, e.g., the larvae of mosquitoes and midges. Many are aquatic, many others terrestrial. Usually the eggs are laid where the larvae will find conditions suitable for their development, and the flies often show such highly developed instincts in this respect that it is hard not to credit them with actual forethought.

The pupae of Diptera also vary widely. In the suborder Orthorrhapha the pupa is protected only by its own hardened cuticle, or, as

in the blackflies, a spun cocoon, and is often capable of considerable activity; from this "obtect" type of pupa (Fig. 204B) the adult insect emerges through a transverse or T-shaped slit, usually near the anterior end. In the suborder, *Cyclorrhapha* the pupa retains the hardened skin of the larva as a protective covering or "puparium" and is usually capable of very slight movement; from this "coarctate" type of pupa (Fig. 204A) the adult escapes by a circular opening made by pushing off the anterior end of the puparium, hence the name *Cyclorrhapha*, meaning "circular slit." Except in a few families (group *Aschiza*) this is done by means of a hernia-like outgrowth on the front of the head. This outgrowth, called the "ptilinum" (Fig. 204C), shrinks after the fly has emerged, but leaves a permanent crescent-shaped mark on the head known as the "frontal lunule" (Fig. 204D), which embraces the bases of the antennae.

The classification of the *Diptera* into major divisions and the characteristics which distinguish the forms that are of medical or veterinary importance are shown in the following key:

Suborder **Orthorrhapha**. Pupa not encased in old larval skin and often active; adults emerge through straight or T-shaped dorsal slit (Fig. 204B); larvae usually with well-developed or somewhat reduced head; wing venation usually fairly simple.

- 1a. Antennae of at least 6 similar joints, and usually long (Fig. 203A, B); larvae with well-developed head; series **Nematocera** 2.
- 1b. Antennae short, with 3 segments, of which the third may show some annulation (Fig. 203E); series **Brachycera** 5.
- 2a. Antennae much longer than head, with distinct whorls of hairs at joints, plumose in males 3.
- 2b. Antennae not much longer than head, with no long hairs (Fig. 203B); body stout and "humped"; wings broad, with only anterior veins well developed (Fig. 211); (blackflies) **Simuliidae**.
- 3a. Body clothed with scales; scales on wing veins and fringe (Fig. 236); (mosquitoes) **Culicidae**.
- 3b. Body and wings without scales 4.
- 4a. Wings with 9 to 11 long, parallel veins, with no cross-veins except at base (Fig. 205); body hairy and mothlike **Psychodidae**.
- 4b. Wing veins not all nearly parallel; body not very hairy; small and short; broad wings fold flat over abdomen, often mottled, anterior veins thickened (Fig. 209); piercing mouth parts **Heleidae**.
- 5a. Third antennal segment annulated, never with a bristle (Fig. 203D, E); a forked vein near tip of wing (Fig. 213A); mouth parts fitted for piercing; wings held apart when at rest; large robust flies **Tabanidae**.
- 5b. Antennae short, with a bristle or style (Fig. 203C); abdomen long and tapering; snipe flies **Leptidae**.

Suborder **Cyclorrhapha**. Pupa encased in old larval skin (puparium) and usually inactive; adults escape through circular split at one end (Fig. 204A); larvae maggot-like without distinct head; wing venation highly modified.

- 1a. No frontal lunule (Fig. 204D) series *Aschiza*.
No bloodsuckers, but includes a few myiasis-producers, *Eristalis* of family
Syrphidae, and *Aphiochaeta* of family Phoridae.
- 1b. Frontal lunule present; series *Schizophora* 2.
- 2a. Opposite legs of each pair close together; abdomen distinctly segmented
(Fig. 266); larval development outside uterus except in tsetse flies; section
Myiodaria 4.
- 2b. Opposite legs of each pair widely separated (Fig. 224); larval develop-
ment in uterus; parasitic; section *Pupipara* 3.
- 3a. Thorax distinct from abdomen; palpi slender and elongate, forming
sheath for proboscis (Fig. 224B); wings often absent; if present, with
stronger veins crowded along costal margin; head and body usually
flattened *Hippoboscidae*.
(1) Wingless; pupae glued to wool; on sheep (sheep tick, Fig. 224C)
Melophagus.
- (2) Winged (Fig. 224A); pupae develop off host; on horses, camels, dogs,
Hippobosca; on birds, *Pseudolynchia*, etc.
- 3b. Palpi broader than long; wing veins not crowded; on bats *Streblidae*.
- 4a. Squamae (or calypteres) rudimentary or absent 5.
- 4b. Squamae well developed 6.
- 5a. Mouth parts vestigial; horse botflies *Gastrophilidae*.
- 5b. Mouth parts normal; wing without subcostal or anal veins, and no closed
cells (Fig. 223) (eye flies) *Chloropidae*.
- 6a. Proboscis well developed; wings about as in Fig. 217A (Muscoidea) 7.
- 6b. Mouth parts vestigial; no palpi; hairy, bee-like flies (botflies); (for key to
genera, see p. 744) *Oestridae*.
- 7a. Proboscis fleshy, fitted for lapping or at most for scratching (Fig. 216,
I and II); arista with lateral hairs, or, rarely, bare; houseflies, fleshflies,
blowflies, screwworm flies. See key on p. 745.
- 7b. Proboscis fitted for piercing 8.
- 8a. Palpi short, not forming sheath for proboscis (Fig. 216, III) (Stable-
flies) *Stomoxys*.
- 8b. Palpi long, capable of sheathing proboscis (Fig. 216, IV) 9.
- 9a. Arista with long feathered hairs on upper surface; wings folded on top of
each other (tsetse flies) *Glossina*.
- 9b. Arista with simple hairs on upper surface; wings diverge when folded
(hornfly) *Siphona*.

SUBORDER ORTHORRHAPHA

Phlebotomus or Sandflies (Psychodidae)

General Account. *Phlebotomus* flies, commonly known as sand-
flies, are minute hairy midges found in nearly all warm and tropical
climates of the world, with the exception of Australia and the East
Indian Islands. They belong to the family Psychodidae, most of which
resemble tiny moths on account of their very hairy bodies and moth-
like pose. They are easily recognized by the characteristic wing vena-
tion, with a series of more or less parallel veins and with no cross-veins

except near the base (Fig. 205*B*). *Phlebotomus* flies hold their wings erect over the body when resting, and are less moth-like than other psychodids.

Theodor (1948) divided the Psychodidae into four subfamilies, of which only the Phlebotominae are bloodsuckers. All of these are

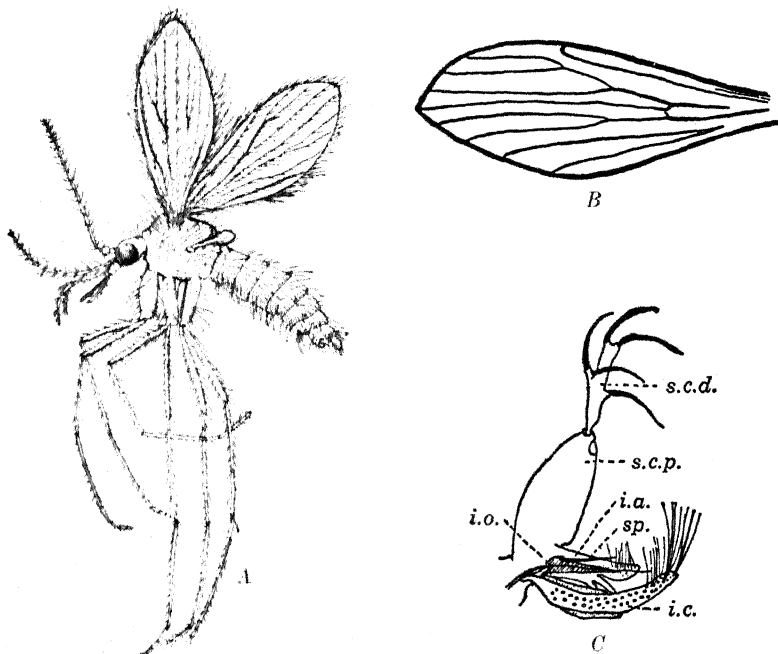


FIG. 205. *Phlebotomus argentipes*: A, adult ♀; B, venation of wing; C, male genitalia; s.c.d., distal segment of superior clasper; s.c.p., proximal segment of superior clasper; i.a., intermediate appendage, with spine (sp.); i.o., intromittent organ; i.c., inferior clasper. (Adapted from Sinton, *Trans. Far Eastern Assoc. Trop. Med.*, 7th Congr., 1928.)

usually included in a single genus *Phlebotomus*; but Theodor recognized four genera, and at least one has been added since. *Phlebotomus*, however, contains nearly all the species that feed on man and other mammals and all that are implicated in the transmission of disease except some South American species, e.g., *Lutzomyia longipalpis*.

Morphology. The sandflies (Fig. 205*A*) are small dull-colored insects, usually yellowish or buff, slender in build, with hairy body, very long and lanky legs, and narrow hairy-veined wings. They have long slender antennae, long maxillary palpi, and a proboscis longer than the head. The proboscis consists of a fleshy labium containing dagger-

like mandibles and maxillae, both with saw-like teeth at the tips; a blade-like hypopharynx containing the salivary duct; and a flat dagger-like labrum-epipharynx which is provided with sensory hairs and spines and is probably not used as a piercing organ. The piercing organs project beyond the tip of the labium when at rest, and the labium does not bow back when the other parts are in action, as it does in mosquitoes. The male genitalia consist of three appendages (Fig. 205C), the details of which are of great value in identification. Other characters useful in classification are details of the palpi, form of the spermatheca, and nature of the pharyngeal teeth. Identification, especially of females, is difficult.

Habits. The females feed exclusively on blood. Their bites are very annoying, causing an amount of irritation quite out of proportion to the size of the insect. The preferred hosts vary with the different species; *Phlebotomus minutus* feeds practically entirely on cold-blooded animals, particularly geckos; *P. argentipes* feeds by preference on cattle and then on man; *P. papatasi*, *sergenti*, and *pernicius* seem to take particular delight in human blood. One Texas species, *P. anthophorus*, has only been found feeding on rabbits, but another, *P. diabolicus*, is an annoying human pest in south central Texas. The males of at least some species appear not to feed at all, subsisting on the remnants of the last larval food. One African species, however, is said to have biting males. Sandflies are very short-lived and seldom survive more than a fortnight. Most sandflies are nocturnal; in some places they seem to forage for only an hour or so after sundown. During the day they hide in dark corners, cellars, crevices of rocks, etc. Their powers of flight are very limited; their range is rarely over 50 yards. When disturbed on walls they usually fly only a few inches, appearing to hop rather than fly. Their breeding places are nearly always within a few hundred feet of their feeding places.

Life History (Fig. 206). Most species of *Phlebotomus* lay their eggs in crevices in rocks, masonry, or crumbling buildings, between boards in privies or cesspools, in rubbish, or in the burrows of animals or in deep soil cracks. The eggs are usually deposited within a few days after emergence and the first blood meal, and vary from 40 to 60 in number; some individuals lay second batches of similar size after a subsequent feed. When deposited, the eggs are literally shot out by the female to a distance several times the length of the abdomen. The eggs are viscid and adhere to the surfaces with which they come in contact; it would seem that the peculiar method of ejecting the eggs is a protective adaptation, facilitating their deposition in the farthest reach of a crevice where even the tiny insect itself could not penetrate. The

eggs are elongate and of a dark, shiny brown color, with fine surface markings which vary in different species (Fig. 206A).

The incubation of the common Old World *Phlebotomus papatasi* requires 6 to 9 days under favorable conditions, but the eggs are very susceptible to external conditions and die quickly if exposed to sunlight or if not kept damp. *P. argentipes* eggs may hatch in 4 days. The larvae (Fig. 206B) are tiny caterpillar-like creatures with a rela-

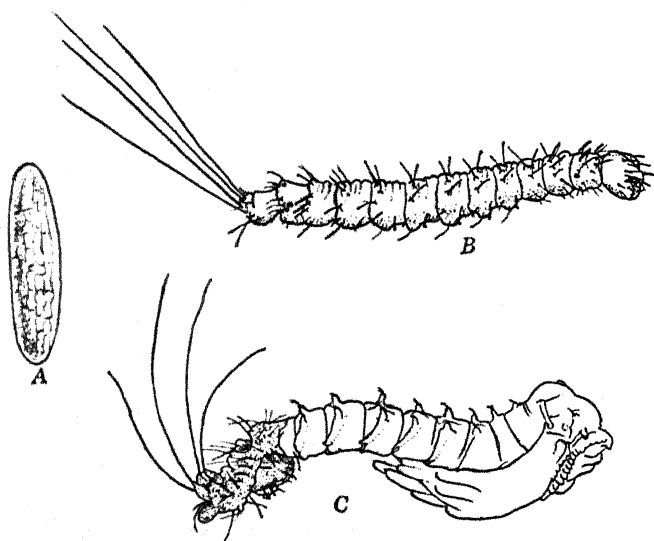


FIG. 206. Life history of *Phlebotomus*: A, egg; B, larva; C, pupa. (Adapted from Patton and Evans, *Insects, Ticks, Mites and Venomous Animals of Medical and Veterinary Importance*, I, Medical, Grubb.)

tively large head and heavy jaws (Fig. 207) and with two pairs of long bristles on the last segment of the abdomen which are held erect and spread out fanwise; in the newly hatched larvae there is only one pair of bristles. The body is provided with numerous toothed spines which give it a rough appearance (Fig. 207). These spines differ in different species and, together with the relative length of the caudal bristles, form good identification marks. The larva of *P. papatasi* when full grown is less than 5 mm. long and it is therefore not so large as an ordinary rice grain.

The larvae feed on decaying vegetable matter, fecal particles, and other organic debris. For all species a high degree of humidity is required, and in the case of *P. argentipes* the wet-bulb temperature must not exceed 80°F. Hibernation probably occurs always in the larval state.

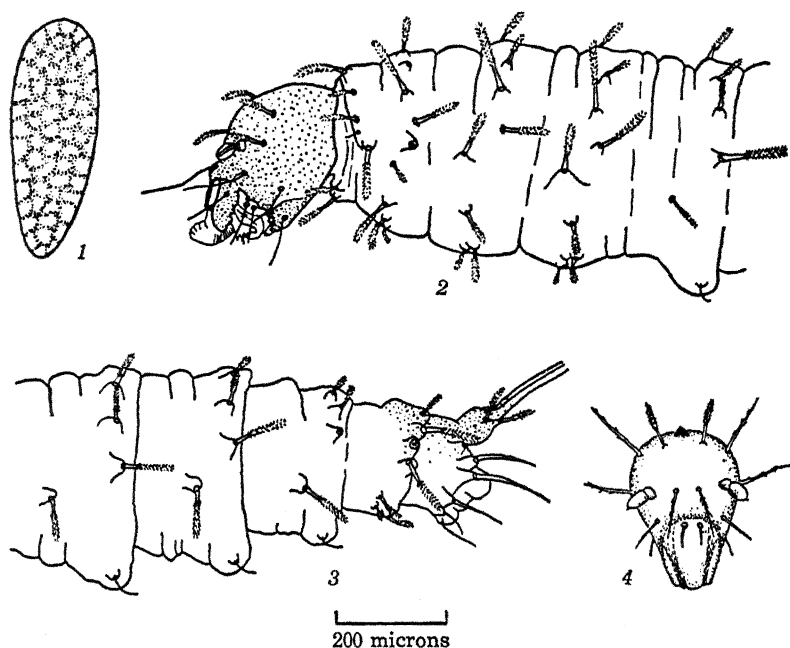


FIG. 207. Egg and larva of *Phlebotomus anthophorus*: 1, egg; 2, anterior end of larva; 3, posterior end of larva (only bases of caudal bristles shown); 4, front view of head of *P. minutus*. (1-3 after Addis, *J. Parasitol.*, 31, 1945.)

The full development of the larvae requires 2 weeks to 2 months or more, depending almost entirely on the temperature. Larvae which hatch at the beginning of cold weather do not pupate until the following spring. The pupa (Fig. 206C) is characterized by a very rough cuticle over the thorax but can be identified best by the last larval skin, which adheres to its posterior end. It is colored much like its surroundings and looks like a tiny bit of amorphous matter. The pupae are less susceptible to drying than the larvae. In warm weather the adult insect emerges after 6 to 10 days, but this is much delayed by low temperatures. The entire life cycle seldom occupies less than 2 months and in cool weather may take several months. Outside the tropics sandflies tend to occur only in rather definite seasons.

SANDFLIES AND DISEASE

Sandflies are of great importance as the transmitters of the various types of leishmaniasis and of a filtrable virus disease called three-day fever, or more commonly sandfly or papatasi fever. Sandflies are also the transmitters of Oroya fever (see pp. 653-654).

Sandfly Fever. This relatively mild virus disease (see p. 233) in many respects resembles dengue and may be confused with influenza. It comes on suddenly with fever, headache, pain in the eyes, stiffness of neck and back, and rheumatic pains. As in dengue, a reduction in white blood cells (leucopenia) is a prominent feature. It is often followed by a prolonged period of malaise and depression. It was experimentally shown by Doerr in 1908 to be transmitted by *Phlebotomus papatasi*. The insects become infective about 6 or 7 days after feeding on a patient in the first or second day of the fever. Since sandflies are so short-lived and frequently suck blood only once, whereas the disease can be transmitted by apparently unfed flies, it had long been suspected that the infection was transmitted to the offspring; Whittingham (1922) proved this to be true by producing sandfly fever by the bites of flies bred from infected parents in England. This transovarial transmission was confirmed in Russia, but not by Sabin et al. (1944). Unless the virus can survive from one season to another in sandfly larvae, its reservoir between seasons is a mystery. No animal except man is known to be susceptible to the virus.

Thus far *P. papatasi* is the only known transmitter throughout the definite range of the disease from Italy to central India, but fevers which may be sandfly fever are reported from the western Mediterranean, tropical Africa, China, and Colombia, and other sandfly vectors are suspected. Sabin et al. isolated two different strains of the virus, from Sicily and the Middle East, respectively. The disease is of little consequence to local populations since immunity is acquired in early childhood, but it may cause serious epidemics in military forces or other non-immune newcomers.

P. papatasi is of medium size, reaching about 2.5 mm. in length. It is pale yellowish gray with a dull red-brown stripe down the middle of the thorax and a spot of the same color at either side. The adult flies choose caves, cellars, catacombs, and similar locations as hiding places. Sandbags used for raising the sides of tents may supply ideal hiding places. On still, warm nights they emerge to feed on human beings who are close at hand, but they avoid even light breezes and can be kept away by ceiling fans. Some houses are found to be much more infested than others, possibly owing to the proximity of suitable breeding places and to the lack of breezes. Dark rooms on the sheltered side of the ground floor of houses are most likely to be infested. The distance traveled by the adults is very short, but they may be carried long distances by public conveyances.

Leishmaniasis. The baffling problem of transmission of the various forms of leishmaniasis (see pp. 137-139) was not finally solved until

1941, but there is no longer any doubt that sandflies are the principal transmitters of all forms of the disease. The species involved in the different forms of leishmaniasis are not the same. The principal transmitters of Oriental sore are *P. papatasi* (see p. 652) and *P. sergenti*, the females of which are almost indistinguishable. Other transmitters are mentioned on p. 140. *P. sergenti* is undoubtedly the most important transmitter in Mesopotamia and India, though *papatasi* appears to play the leading role in north Africa, and *P. perfliewi* in Italy. The last species breeds in dung heaps; if these are over 100 yards from houses there is little or no Oriental sore.

The species primarily concerned in transmission of the American forms of dermal leishmaniasis are not well known, although in Brazil there is evidence against *P. intermedius* (see p. 150), and also *P. migonei* and *pessoai*.

Most of the species concerned with kala-azar in the Old World belong to the *P. major* group. In India it is *P. argentipes*, a species about 2.5 mm. long, grayish with silvery white tarsi. The adults feed by preference on cattle but attack man when cattle are not readily available. The fly is very local in distribution, being found especially in masonry or thick mud-walled houses and rarely in thin-walled bamboo-and-plaster huts. The adults live only 3 days without food and usually die after the first oviposition, when about 50 to 60 eggs are laid. The adults fly only a few yards, are strictly nocturnal, and never rise to the second floor of a building. In China *P. chinensis* becomes infected readily after feeding on infected hamsters (*Cricetulus griseus*) and is probably the natural vector. This species seems to have but one brood a year. *P. perniciosus* and *P. major* are the probable natural transmitters of the Mediterranean infantile and canine types of kala-azar. Proboscis infections, however, are rare and occur only late in the season, a fact which may have some bearing on the epidemiology of the disease (see p. 142). *P. perniciosus* is much less frequently found in houses than is *P. papatasi*. In South America the parasites of visceral leishmaniasis develop readily in both *P. intermedius* and *P. longipalpis* when these flies are fed on infected dogs.

Oroya Fever. Oroya fever or Carrion's disease is an acute febrile disease caused by a very minute organism, *Bartonella bacilliformis* (see p. 231), occurring in valleys on the slopes of the Andes in Peru, Chile, Ecuador, and Bolivia. In 1938 it appeared in epidemic form in the province of Nariño in Colombia, causing 1800 deaths in 9 months in a population of perhaps 200,000. The acute stage of the disease is characterized by high fever, severe anemia, aches, and albuminuria, and is often fatal. In more chronic cases it is followed by an eruption

of nodules called verruga peruviana. In mild cases the eruption may be the only manifestation, and it is considered a good sign when it appears. Some cases seem to be symptomless. Geiman developed good culture media for the organism, making possible an agglutination test for diagnosis.

The probable relation of sandflies to this disease was pointed out by Townsend in 1913. In the Peruvian Andes the disease is limited to a comparatively small zone and is contracted exclusively at night. *Phlebotomus verrucarum* is the principal, probably the sole, transmitter. It is a strictly nocturnal species which enters houses readily and bites man freely. In Colombia the transmitter is believed to be *P. colombianus*, possibly merely a variety of *P. verrucarum*; the females of these two species are indistinguishable. What the natural source of *Bartonella* infections in sandflies is and how the organisms develop in them are still unsolved questions (see Hertig, 1942, 1948).

P. verrucarum is found in the deep-cut canyons of the west slope of the Peruvian Andes at elevation between 2800 and 8000 ft. Within this zone it would be extremely dangerous to be caught at night, for no ordinary screening would afford adequate protection. At lower elevations the valley is too arid for sandflies to breed, and at higher elevations the cold nights inhibit their activity. In the verruga zone there is a favorable combination of cool summers, warm sunny winters, moderate rainfall, and mild nights—a zone of perpetual spring.

CONTROL

Because of their short flight range, which is seldom over 75 to 100 yd., and their tendency to stay close to the ground, sandflies are very easily controlled locally by DDT sprays. Spraying the inside and outside of houses, rock walls, etc., eliminates them for months. The long life cycle results in a very slow comeback of a depleted population. Remarkable results in sandfly control have been reported by Hertig and Fairchild (1948) in Peru and by Hertig (1949) in Greece, Crete, Italy, and Sardinia. In compact communities one annual pre-season house spraying is sufficient to reduce sandflies to near the vanishing point.

When venturing beyond protected areas after sundown it is necessary to use protective clothing and repellents, of which dimethyl phthalate is probably best.

Biting Midges or No-see-ums (Heleidae)

Morphology. The tiny flies belonging to this family (Fig. 208) go by various names: midges, gnats, punkies, or sandflies, and, in the

west, "no-see-ums" because of their minute size, which is seldom over 1 to 2 mm. in length. They can usually be distinguished from allied insects by the peculiar venation of the wings, the first two veins being very heavy whereas the others are more or less indistinct. The scales so characteristic of mosquitoes are absent. The proboscis is short and essentially similar in structure to that of *Simulium* (Fig. 211B); one

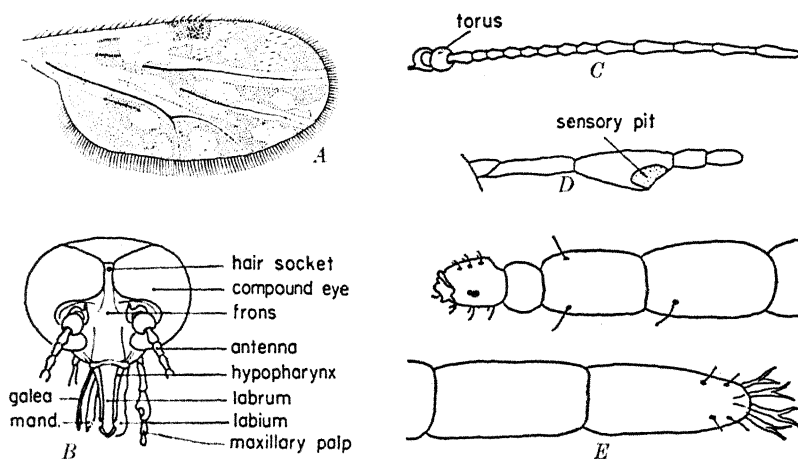


FIG. 208. *Culicoides*. A, wing of *C. furens*; B, head; C, antenna; D, maxillary palp; E, anterior and posterior ends of larva of *C. furens*. (A-D, after Foote and Pratt, *Publ. Hlth. Mon.* 18, 1954; E, after Painter, *Med. Dept. United Fruit Co.*, 15th. Rept., 1927.)

marvels at the irritation which can be inflicted by such a small insect with such a small organ. The maxillary palpi have 5 joints, the third enlarged with a characteristically placed sensory pit (Fig. 208D). The antennae are long, with 13 segments in the filament; in the males they are more plumose with the last 3 or 4 segments lengthened; in females they are filamentous with the last 5 segments differing in character from the others. In most species the wings are mottled in characteristic patterns (Figs. 208A and 210). The male genitalia are useful in identification of species.

The family includes many genera (see Johannsen, 1943), but the majority of species that attack man and animals belong to the genus *Culicoides*. There are, however, some annoying pests in the genera *Leptoconops*, *Helea* (= *Ceratopogon*), *Forcipomyia*, and a few others.

Habits and Life Cycle. Only the females are bloodsuckers. They become active at dusk, but if disturbed many of them will bite in the shade, even on bright days. Both sexes are attracted by lights. They

are much more active fliers than *Phlebotomus*, and are said to go as far as half a mile in search of a host, but only when the air is still. Most of the species appear to prefer cattle, camels, or other animals as food, but some species readily attack man.

The eggs of *Culicoides*, several hundreds in number, are deposited in gelatinous masses like miniature masses of frog eggs and are usually

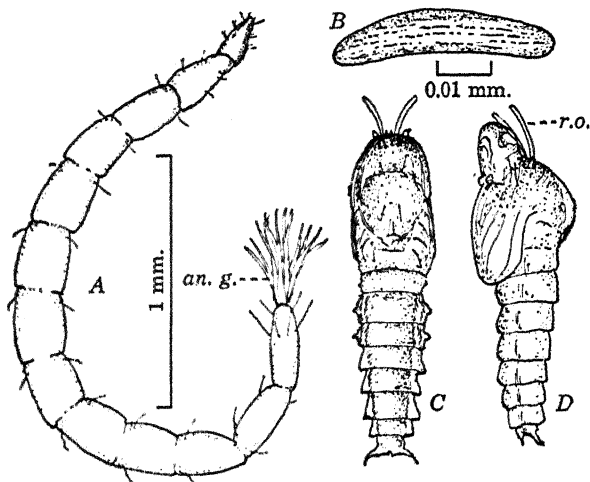


FIG. 209. Immature stages of *Culicoides*. A, larva (the anal gills (*an.g.*) are retractile, there is no proleg, and the anal segment has three pairs of hairs); B, egg, much enlarged; C and D, dorsal and lateral views of a pupa; note slender respiratory organs (*r.o.*) on thorax. (After Dove, Hall and Hull, *Ann. Ent. Soc. Amer.*, 25, 1932.)

moored to some object under water in swamps, ponds or tree holes; some species breed in rotting vegetation. Relatively cool shaded places are preferred by most species. Some species favor brackish or salt water.

After a few days slender larvae (Fig. 209A) hatch. They burrow in decaying vegetation or mud either in or out of water, according to the species. When swimming, their movements suggest giant spirochetes. *Culicoides* larvae, unlike the related chironomid larvae, do not have pseudopods on the first or last segments of the abdomen. At the posterior end there are gill-like structures that can be protruded; the larvae do not need air as do mosquito larvae. The food of most species consists of microscopic plant and animal life or organic debris. The pupa (Fig. 209C, D) rather resembles that of a mosquito, except that the abdomen is kept extended instead of curled under and the pupa hangs from the surface in a vertical position, breathing through

a pair of trumpet-like tubes as do mosquitoes. Both larvae and pupae are hard to find, and the presence of a breeding place is more frequently discovered by finding the floating pupal cases from which the adults have emerged.

Dove et al. (1932) believe that the larvae of *C. furens* (which they called *dovei*), a pestiferous salt marsh species and filarial vector (see below), may live for 6 months to a year. *C. austeni* of Africa, however, has an egg-to-adult cycle of 25 to 28 days. In contrast, *C. tristriatulus* of Alaska has one brood a year, the larvae living through the winter buried in soil.

Annoyance. The bites of *Culicoides* produce nettle-like pricks which are sometimes followed by burning sensations and intolerable itching; in many sensitized individuals the bites last longer and are more painful than mosquito bites, but eventually most people develop some degree of immunity to them. The ability of these insects to go through ordinary mosquito screens makes them particularly obnoxious. Some species are so minute as to be individually overlooked, but they may be so abundant as to give a gray tinge to the skin and to cause extreme irritation. Dove et al. (1932) think the flies are attracted by the heat emanating from warm bodies, but the writer believes they are attracted largely by animal odors, since he has been attacked by great swarms upon opening a rabbit carcass. The flies usually attack exposed parts of the body but will bite through thin clothing. Salt-marsh breeders (*C. furens* and others) are intolerable pests along the southern Atlantic seaboard of the United States, so much so as to have retarded development of certain areas. They seriously interfere with romance on moonlit beaches in the West Indies and Central America.

MIDGES AS DISEASE CARRIERS

Culicoides serve as intermediate hosts for three filarial worms of man, *Dipetalonema perstans*, *D. streptocerca*, and *Mansonella ozzardi*, and at least two filariae of animals, *Onchocerca reticulata* of horses and *O. gibsoni* of cattle. In addition, *Culicoides* have been accused of transmitting several virus diseases: blue tongue of sheep and "horse sickness" in South Africa, and fowlpox of poultry in Japan. Two land-breeding species, *Forcipomyia utae* and *F. townsendi* were believed by Townsend to act as transmitters of uta, a form of leishmaniasis in Peru, but this work needs confirmation.

***Culicoides* and Filarial Infections.** Sharp (1928) proved two species of *Culicoides*, *C. austeni* (Fig. 210) and *C. grahami*, to be intermediate hosts of the filarial worm, *Dipetalonema* (= *Acanthocheilonema*) *perstans* (see p. 475) in British Cameroons, where over 90 per cent

of the natives are infected in some areas. This was later confirmed by Hopkins and Nicholas (1952), although work by Chardome and Peel (1949) in Belgian Congo threw doubt on it (see p. 476). The latter workers showed that *C. grahami* was an intermediate host for *Dipetalonema streptocerca* in that country.

C. austeni is a night-biting fly which is abundant in villages in or near rain forests, readily entering houses to bite in darkness, but often leaving again during the night. A blood meal is necessary before eggs

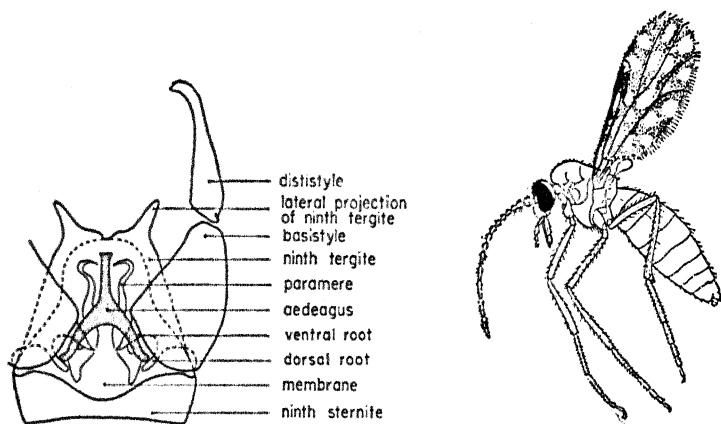


FIG. 210. Left, diagram of δ genitalia of *Culicoides* (after Foote and Pratt, *Publ. Health Mon.* 18, 1954). Right, *Culicoides austeni*, vector of *Dipetalonema perstans*, $\times 20$ (after Sharp, *Trans. Roy. Soc. Trop. Med.*, 19, 1928).

are laid. Breeding is common in banana stumps in early stages of decay, which tends to increase the density of the insects near villages; undoubtedly there are other breeding places in the forests. The flies appear to disperse not over 400 yards from their breeding places in clearings, but their dispersal may be different in the forest canopy. *C. grahami*, a smaller species (1 mm. long as compared with 2 mm. for *austeni*), bites in early morning and evening, or all day on dark, rainy days. It also breeds freely in banana stumps and frequents villages, but it is commoner than *austeni* in forest reserves, grasslands, and transition areas. It is a less efficient vector than *austeni*, but may nevertheless be important under some circumstances.

Buckley (1934), working on the island of St. Vincent, W. I., showed that a *Culicoides*, *C. furens* (Fig. 208), serves as an intermediate host for another filarial worm, *Mansonella ozzardi* (see p. 476). The development in *Culicoides* is similar to that of *Dipetalonema perstans*. *C. furens*, a notorious biter, is a brackish-water breeder.

It is easily recognized by the speckled appearance of the mesonotum. It is widely distributed on the Atlantic and Gulf coasts from Massachusetts to Texas, Mexico, West Indies, and Brazil, and is the most troublesome species in Florida.

Steward in 1933 showed that *Onchocerca reticulata*, the cause of fistula of the withers or head (poll-evil) in horses, is transmitted by *C. nubeculosis* in England. This species breeds in liquid manure and other foul stagnant water. Buckley (1938) showed that in Malaya *Onchocerca gibsoni* of cattle can undergo development to the infective stage in several species of *Culicoides*; although less than 0.5 per cent of the flies were successful hosts, the flies were so numerous that Buckley calculated that a cow would be bitten by at least one infective fly every day. Circumstantial evidence points to *Culicoides* as vectors of *O. gibsoni* in Australia and South Africa. Attempts to get development of *O. volvulus* of man and *O. gutturosa* of cattle have failed.

CONTROL

The control of *Culicoides* is often difficult, and the methods must depend on knowledge of the breeding places of the species to be controlled. Marsh-breeding species, such as *C. furens*, may sometimes be reduced 90 per cent by draining, ditching, or diking. Good control of this species was reported by spraying Dieldrin emulsion with ground equipment; 1 lb. per acre was effective for 20 to 40 weeks, and 2 lb. for 65 weeks. DDT, however, is quickly detoxicated by mud so is less effective than it is against mosquitoes. In England a BHC emulsion, applied at 100 mg. per square foot, gave good results in small breeding areas, especially when rain caused deep penetration; preseason spraying was suggested. Spraying or painting DDT solutions on screens and on resting places near habitations is helpful. Thermal aerosols are useful for temporary emergency treatments. Repellents (see p. 519) are effective for shorter periods than for most insects. In Africa it seems that considerable protection against the *C. austeni* and *grahami* might be obtained by elimination or treatment of banana stumps near villages.

Blackflies or Buffalo Gnats (Simuliidae)

The blackflies, as annoyers of domestic animals and man, are among the most important of insect pests, since they often appear in overwhelming hordes. The females are most vicious bloodsuckers, and in especially bad outbreaks they may kill large numbers of animals. A famous migratory European species, *Simulium colombaschense*, killed 16,000 domestic animals in 1923 and about 14,000 in 1934 in the

Balkans. Unlike most small biting flies, blackflies are diurnal. They have a world-wide distribution, being found from the arctics to the tropics and up to perpetual snow on mountains, wherever there is running water.

The Simuliidae were split by Smart (1945) into half a dozen genera, largely on the basis of wing venation. Three genera are represented by common species in North America: *Prosimulium*, containing *P. hirtipes*, a springtime pest in the northeast; *Cnephia*, containing the buffalo

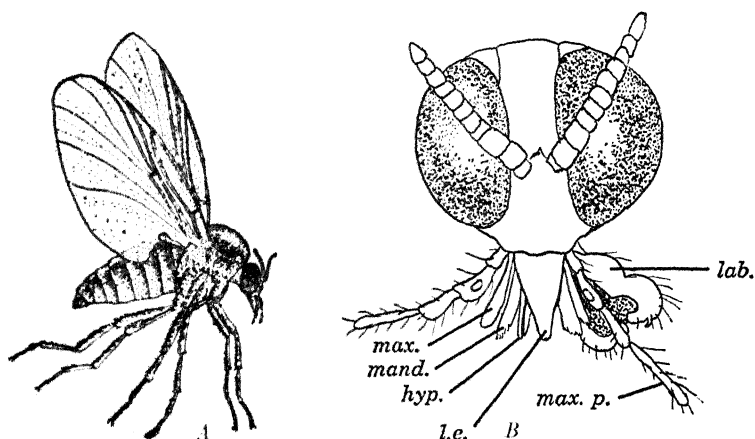


FIG. 211. A, Blackfly (buffalo gnat), *Cnephia pecuarum*, $\times 7$ (after Riley). B, Mouth parts of *Simulium*: hyp., hypopharynx; lab., labium; l.e., labrum-epipharynx; mand., mandible; max., maxilla; max.p., maxillary palpus (after Alcock, *Entomology for Medical Officers*, 1920).

gnat, *C. pecuarum* (Fig. 211), tormentor of man and animals in the South Central States; and *Simulium*, containing *S. venustum*, a scourge in the eastern parts of the country, and *S. arcticum* of the northwest. The genus *Simulium* contains the great majority of the species, including all the important transmitters of disease.

Morphology. Unlike the usual slender, midge-like flies with long legs and long antennae in the group Nematocerca, the blackflies are small, robust, hump-backed creatures with short legs, broad wings, and short, eleven-jointed antennae without whorls of hairs at the joints (Fig. 211A). The proboscis in the female is short but heavy and powerful; in the males, which are not bloodsuckers, it is poorly developed. The mouth parts (Fig. 211B), consisting of toothed dagger-like mandibles and maxillae, and also a hypopharynx and labrum-epipharynx, resemble in general those of *Phlebotomus*.

Most of the northern species are black, whence their name, but

some of the species are reddish brown or yellowish, and they may be variously striped and marked. The wings are either clear or of a grayish or yellowish color, with the few heavy veins near the anterior margin often distinctively colored. Some of the species are not more than 1 mm. in length, and the largest of them scarcely exceed 4 mm.

Life History and Habits. Unlike the mosquitoes and midges, blackflies breed in running water, and few streams flow too swiftly for

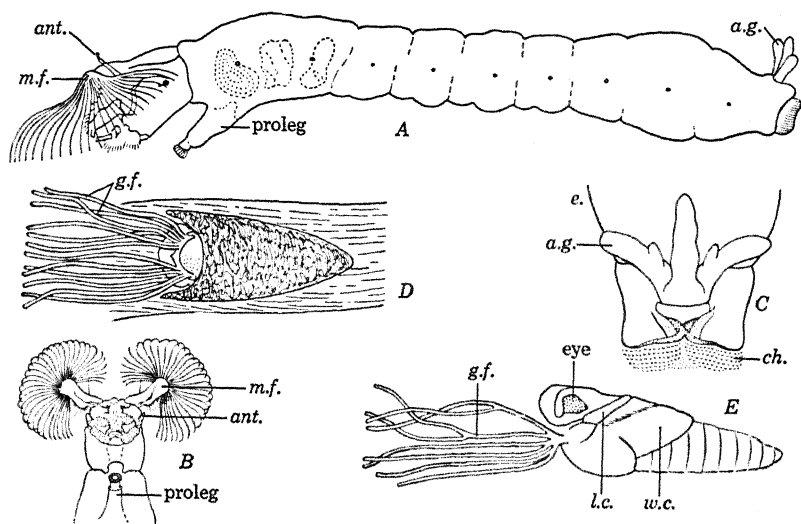


FIG. 212. Developmental stages of *Simulium*. A, larva; B, anterior end of larva, ventral view; C, posterior end of larva, dorsal view; D, wallpocket-like pupal case, with gill filaments of pupa protruding; E, pupa: a.g., anal gills; ant., antenna; ch., caudal circlets of hooks; g.f., gill filaments; l.c., leg case; m.f., mouth fan; w.c., wing case. (A and B, adapted from Peterson, *Larvae of Insects*, pt. 2, 1951. C from Brumpt, *Précis de parasitologie*, 1940. D and E from Jobbins-Pomeroy, *U. S. Dept. Agric. Bull.* 329, 1916.)

them. The eggs (Fig. 212A), which have a peculiar slimy coating, are laid in masses of 200 to 300 per female. In some species numerous females hover over a stream, repeatedly darting into the water or to an emergent rock or leaf to oviposit, thousands of eggs thus accumulating in one area.

The choice of breeding places varies; some prefer large rivers, some bubbling brooks, some trickling streams. The larvae of some are found on rocks, boards, etc., on the bottom, some on vegetable debris or emergent vegetation licked by the water, and some, e.g. *S. neavei* (see p. 664), only on the shells of crabs. The famous Columbacz fly of the Balkans, *S. colombaschense*, breeds down to a depth of 190 ft. in the Danube in Yugoslavia.

The larvae, which hatch in a few days, cling to objects in even very swift water by means of circles of minute hooklets at the blunt posterior end of the body; they avoid objects coated by algae or slime, or hairy plants. They spin glutinous silken threads from modified salivary glands which extend to the posterior end of the body; these threads serve for anchoring and as life lines, and are also used to spin cocoons. The larvae have a stumpy proleg (Fig. 212, *pl.*), also provided with hooks, and by using this and the posterior circlet of hooks they loop along like "measuring worms." There are a pair of "mouth fans" by means of which microscopic organisms are swept into the mouth. The larvae breathe by means of tiny gills that can be projected through the anal slit in the last segment of the abdomen.

When ready to pupate the larvae spin for themselves a partial cocoon which is variously shaped like a jelly glass, slipper, wall pocket, etc., open at the upper end for the extrusion of the branching gill filaments which are used as breathing organs (Fig. 212*D*). Some species simply spin a snarl of threads, the work of a whole community, in the meshes of which the pupae exist in a fair state of protection. The general form of the pupae can be seen in Fig. 212*E*. The breathing filaments vary greatly in different species and may have four to sixty branches. The adults emerge in 3 days to a week or more and are carried to the surface by a bubble of air which has been collected inside the old pupal skin. The adults are short-lived and lay their eggs soon after emergence.

The far northern species have only one or possibly two broods a year, most of them coming out in devastating hordes for a few weeks in late May or June after overwintering as larvae; but in warmer climates there are several broods and in the tropics many, the generation time being only about 3 or 4 weeks. Here survival of a dry season is the problem; some evidence indicates that adults seek shelter in rock crevices in dry stream beds, but it is also possible that resistant eggs may be laid. In the tropics the eggs may hatch in 2 days, the larvae go through 6 molts and pupate in 5 to 7 days, the adults emerge from pupae in 4 days, and the adults lay eggs in 4 days more (Wanson, 1950). In some and probably all species a blood meal is necessary before development of the eggs.

The adults, at least in Guatemala, are not found resting in grass or bushes, but high up in trees. Nearly all species travel for considerable distances. *S. damnosum* in Africa may migrate up to nearly 50 miles from its breeding area, and it commonly goes 6 to 12 miles. In Guatemala recaptured dyed flies had flown an average of about 7½ miles. In the Balkans swarms of the *Columbaez* fly rise high in the air and are

carried by air currents 100 miles or more, after which they come down and begin an active migration covering 3 to 6 miles per day, killing many unprotected animals on their way. Blackflies feed only in fairly bright light, and so do not bite in dark habitations. In poor light, white-skinned people may be bitten when dark-skinned ones are not.

In contrast to such insects as mosquitoes and tabanids, blackflies are slow biters, requiring an average of about 5 to 7 minutes to engorge. The bites are usually not immediately painful; they bleed at first, and after several hours begin to swell and become more agonizingly itchy for about 3 days, when the annoyance is almost intolerable. A feeling of malaise and despondence, with some fever, may also develop. Fortunately repeated attacks convey some degree of immunity but, as with other immunities of this sort, it is much more effective in some individuals than in others. The slow development and toxic nature of the symptoms suggests injection of a virus, but similar effects can be produced by injection of material from preserved flies. Apparently the salivary secretion is particularly toxic. Animals, and even children, may be killed not only by the irritation and loss of blood, but even by choking from hordes of flies entering through the nostrils.

Blackflies, like other groups of biting flies, vary greatly from one species to another in their blood preferences, some confining their attacks largely to birds or cold blooded animals, and some to large mammals. Comparatively few habitually attack man. Bequaert in 1938 said that of 57 species known in Africa only 5 have been reported as biting people. In Mexico and Guatemala *S. ochraceum* seems to be the only truly anthropophilic species, but a number of others (*metallicum*, *callidum*, *exiguum*, *haematopotum*, and *veracruzianum*) have no marked aversion to human blood. In Africa *S. damnosum* and *S. neavei*, the two vectors of onchocerciasis, are the only species that really prefer human blood, and even *S. damnosum* avoids biting man in some localities. In a part of Sudan (Dongola) *S. griseicollis* is an important human pest even though only a small proportion of the flies molest man, for there are countless numbers of them. A few of the commoner man-biters in North America were mentioned above. Some species almost always bite on the legs, whereas some, e.g. *ochraceum*, bite the upper parts.

SIMULIUM AND DISEASE

Onchocerciasis. Blacklock (1926), working in Sierra Leone in Africa, first showed that the important filarial parasite of man, *Onchocerca volvulus*, was transmitted by a blackfly, *Simulium damnosum*.

Subsequently *S. neavei* in Africa and several species in southern Mexico and Guatemala were found to be important vectors.

The flies appear to exert a chemotactic attraction on the microfilariae in the skin, so that as many as 100 to 200 may be ingested during engorgement. Most of these are held in the fly's gut by the peritrophic membrane that is secreted during feeding (see p. 506), so only a few (average three in *damnosum*) succeed in developing. Too many larvae kill the flies, and even a few developing in the thoracic muscles tend to retard flight and perhaps hasten death. Unlike infective filarial larvae in mosquitoes and *Chrysops*, *Onchocerca* larvae may not lie in wait in the proboscis but, stimulated by the warmth, migrate from the body cavity of the fly during the slow engorgement.

Food habits constitute the most important factor in determining which species are important vectors of onchocerciasis, but some species seem to be poor hosts for the worms, and others are unimportant because they nearly always bite on the legs.

Of the American transmitters, as noted on p. 479, *S. ochraceum* is most important, although other man-biting species (*metallicum*, *callidum*, *veracruzianum*) may be locally important. Finding flies naturally infected with *Onchocerca* larvae may be misleading, for in some areas in the onchocerciasis zone 100 per cent of cattle are infected with *Onchocerca gutturosa* and a high proportion of horses with *O. reticulata*. *S. ochraceum* is a small species 1.5 to 2 mm. long, with yellowish-red thorax, black legs, and yellow and black abdomen. It breeds only in permanent, shaded, spring-fed streams, some of them mere trickles, where there is emergent and overhanging vegetation—what Elishewitz (World Health Organisation Expert Committee Report, 1953) calls "young" streams. It never breeds in older streams which have beaches and are not overhung by vegetation. Since these "young" streams are limited to a zone between about 4200 and 2000 ft. elevation, the important onchocerciasis zone is also limited, though extended somewhat by migration of the flies. Zoophilic blackflies breed mainly in "mature" streams, primarily on rocks rather than vegetation.

In Africa only *S. damnosum* and *S. neavei* are vectors. The former is widely distributed south of the Sahara and breeds in large rivers as well as in smaller tributaries not choked by papyrus, preferring rapids or cataracts of broken water, but breeding also in stretches where the current may be only 2 or 3 miles per hour. The eggs are laid on partially submerged objects, and the larvae attach to stones, vegetation, etc., at various depths. The adults are abundant where there is high grass or dense vegetation along the river banks, and also at distant places. *S. neavei*, confined to central Africa, lays its eggs in clusters

on vegetation, but the larvae and pupae are found only on the shells of crabs of the genus *Potamonautes*, which live in sunny cascades and rocky falls in rivers, usually at elevations of 1400 to 2000 ft. The larvae probably benefit from particles of food torn up by the crabs. The adults congregate in humid forests, whence they make short sorties to bite.

In Europe *S. ornatum* is a transmitter of *Onchocerca gutturosa* of cattle, but the transmitters of this and of other *Onchocerca* infections in animals elsewhere have not been determined.

Leucocytozoön Infections of Birds. O'Roke (1934) found *Simulium venustum* to be the intermediate host of *Leucocytozoön simondi* (see p. 184), which causes a malaria-like disease of ducks in northern United States serious enough to prevent the raising of them in some localities and undoubtedly very injurious to wild ducks. This species also transmits *L. bonasae* of ruffed grouse. *S. jenningsi* (= *nigroparvum*), *S. slossonae*, and *S. occidentale* transmit a similar destructive disease of turkeys caused by *L. smithi*. This disease and its transmission by blackflies have been observed in Nebraska, Virginia, and South Carolina, where in some places 100 per cent of young turkeys become infected and 5 per cent die.

CONTROL

DDT has proved a very effective insecticide for destruction of black-fly larvae. One part in 10,000,000 of water maintained for 15 to 30 minutes is destructive. This high effectiveness is believed by Hadaway and Barlow (1952) to be due to adherence of the emulsion particles to diatoms, alga spores, etc., which are ingested by the larvae. Some astonishing successes have been obtained. Wanson et al. (1948) eradicated blackflies from the Congo at Leopoldville by airplane spraying; Barnley (1953) reported success on the Victoria Nile for a distance of 42 miles by applying 11 weekly doses to give a 30-minute contact at a final dilution of 1 : 2,000,000. Within an hour the larvae could be seen streaming away on their silken webs, and next morning no live larvae could be found. In 2 weeks algal growths covered the rocks, and no *S. damnosum* larvae were again found until nearly 5 months later; the adult fly density dropped dramatically about 10 days after the first application. Garnham and McMahon (1947) eradicated *S. neavei* from a district in Kenya, and it was still absent 7 years later. Fairchild and Barreda (1945) demonstrated effective control in Guatemala, as did Elishewitz in 1944 (see W.H.O., 1953). Although application of emulsions over a period of time seems to give best results, airplane dusting or use of briquettes, etc., soaked in DDT solutions

are indicated in some places. Effective use of airplanes has been reported in Alaska and Pennsylvania.

Protection against blackflies can be obtained by the use of repellents (see p. 519), particularly dimethyl phthalate. Few blackflies enter houses, and they do not bite in dark places. DDT thermal-generated aerosols (see p. 518) are also helpful. In camp life and for the pro-

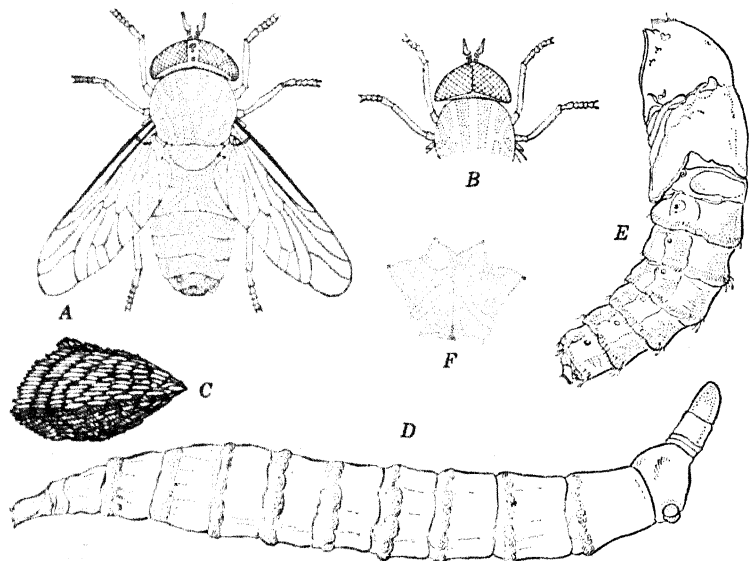


FIG. 213. Life cycle of tabanids. A, adult (*Tabanus vivax* ♀); B, head of ♂ (note spacing of eyes); C, egg mass; D, larva; E, pupa; F, "aster" at posterior end of pupa. (A, B, and F adapted from Hines, *U. S. Dept. Agric. Misc. Papers, Tech. Ser.*, 12, pt. 2, 1906. D and E from Patton and Evans, *Insects, Ticks, Mites and Venomous Animals of Medical and Veterinary Importance*, Grubb.)

tection of animals in pastures smudges are indispensable. The flies will not tolerate the smoke, and domestic animals soon learn to take advantage of its protection. Cheap repellents made of emulsions of kerosene or various resinous oils with soap and water have also been recommended for spraying animals.

Horseflies (Tabanidae)

The tabanids are the only Brachycera (see p. 646) which suck blood except some species of the family Rhagionidae (=Leptidae), the snipe flies. One genus of these, *Symphoromyia*, contains vicious blood-suckers in North America, but they are not known to transmit disease. These flies have a long tapering abdomen, and antennae with a terminal

bristle (Fig. 203C). The tabanids, known as gadflies, deerflies, horseflies, etc., are mainly animal pests, but many species attack man also, inflicting painful bites. They are also implicated in the spread of certain diseases of man and animals. The females alone are blood-suckers, the males living chiefly on plant juices; even the females in some genera feed on flowers. These flies, of which over 2500 species have been recorded, occur in every part of the world, but the species are most abundant in warm climates.

Morphology. The tabanids are of large size and heavy build (Fig. 213A). They are often beautifully colored in black, brown, and

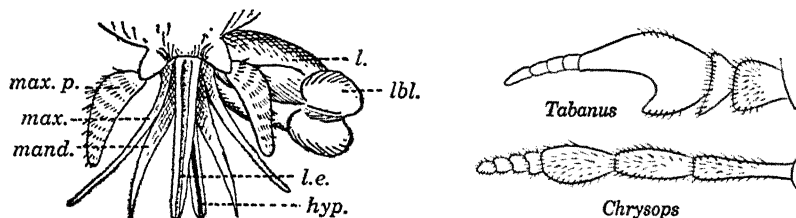


FIG. 214. Left, mouth parts of a tabanid; *hyp.*, hypopharynx; *l.*, labium; *lbl.*, labellum; *l.e.*, labrum-epipharynx; *mand.*, mandible; *max.*, maxilla; *max.p.*, maxillary palpus. Right, antennae of *Tabanus* and *Chrysops*.

orange tones, sometimes with brilliant green, or green-marked eyes, though in most species of temperate climates the huge eyes are brown or black. The head is large and in the male is almost entirely occupied by the eyes, which meet across the crown of the head; in the females a narrow space is left between them. The antennae are of characteristic shape (Fig. 203D, E), varying somewhat in the different genera. The mouth parts (Fig. 214, left) are almost exactly like those of the blackflies on a large scale. The stabbing and cutting parts are usually short, heavy, and powerful, though in one genus, *Pangonia*, the proboscis is very long, enabling the fly to pierce even through thick clothing. The wings are usually held at a broad angle to the body, as shown in Fig. 215; they have a characteristic forked vein near the tip, and often have smoky markings which help in identification.

Of the four genera most important as human pests, *Tabanus* (Fig. 213) is large and has clear or smoky wings, with no spots or a few small scattered ones; *Pangonia* also has clear or smoky wings but can be distinguished by the long proboscis; *Haematopota* is of moderate size and has wings with profuse scroll-like markings; and *Chrysops*, the species of which are often even smaller than a housefly, has conspicuous black bands and spots on the wing (Fig. 215).

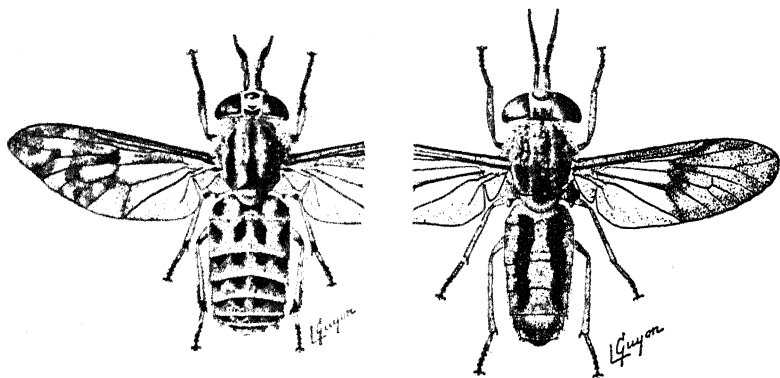


FIG. 215. Left, *Chrysops discalis*, the vector of deerfly fever. Right, *Chrysops dimidiatus*, vector of Lou lou. (After Brumpt, *Précis de parasitologie*, Masson.)

Life History and Habits. All the tabanids breed in water or in damp places. The eggs (Fig. 213C), several hundred in number, are laid in definitely shaped masses on the leaves of marsh or water plants, on the leaves or twigs of trees overhanging breeding places, or in crevices of rocks along the sides of streams. When deposited the eggs are covered by a gluey waterproof secretion that binds them together; they are white at first but soon turn dark. They are deposited during the summer or wet season and under favorable circumstances hatch in 4 to 7 days. Many are attacked by small hymenopteran parasites.

The newly hatched larvae fall into the water or to wet or damp ground. The larvae (Fig. 213D) are cylindrical legless creatures, tapering at each end. The body has eleven segments exclusive of the very small and often retracted head. Each segment has a row of wart-like processes provided with spines or hairs. The larvae are voracious feeders; most species prey upon soft-bodied animals such as earthworms and insect larvae and are not averse to cannibalism if food is scarce, but most species of *Chrysops* feed on dead organic matter. The larvae are active and grow rapidly during the summer, but in winter in the north they bury themselves several inches deep in soil or dead vegetation, which may freeze around them. In the spring the mature larvae migrate to drier ground and pupate. The pupae (Fig. 213E) are suggestive of the chryalids of butterflies. Many species are recognizable by the characters of the "aster" (Fig. 213F) at the posterior end. The pupal period lasts only 1 to 2 weeks. Some tabanid larvae may take 3 years to mature. In the tropics a buried resting stage during the dry season has been suggested. Most species have but one brood a year and are seasonally abundant.

Nearly all tabanids are diurnal, and often active in bright sunlight, though some species prefer shade and a few in central Africa are said to extend their activities into the night. They are strong fliers, and may travel a mile or more from their breeding places. Most species are very deliberate in their feeding, and not easily disturbed after beginning a meal. They like to skim over the surface of water, a habit that can be taken advantage of to trap them in oil-covered pools.

Annoyance and Damage. Tabanids cause serious injury to cattle by annoyance and loss of blood, the latter easily amounting to 100 to 200 cc. per day. This, together with loss from *Stomoxys* and hornflies (see pp. 672 and 673), is sufficient seriously to reduce weight gain and/or milk production. Animals may gain 20 to 25 lb. and increase their butterfat production by 15 per cent within a month after being freed from annoyance by tabanids. Even human beings may suffer severely from bites of tabanids, particularly deerflies.

TABANIDS AND DISEASE

Trypanosomes. Tabanids are of importance in connection with the transmission of some of the trypanosomes of animals. *Trypanosoma evansi*, causing surra in horses, cattle, camels, dogs, etc., and the related *T. equinum*, causing mal-de-caderas of horses and other animals in South America, are commonly transmitted by tabanids and *Stomoxys* from one animal in a herd to another by a soiled proboscis. Even the tsetse-borne trypanosomes are frequently transmitted in this manner (see p. 176), especially *T. vivax*, which has become established outside of tsetse areas in Africa, and even in South America. Trypanosomiasis of man are probably much less frequently transmitted by tabanids and *Stomoxys* than are those of animals. At least one species of trypanosome, the non-pathogenic *T. theileri* of cattle, undergoes cyclical development in tabanids.

Tularemia. In the western United States, particularly in Utah and Colorado, there is a form of tularemia known as "deerfly fever," which seems to be associated with the bites of a single species of deerfly, *Chrysops discalis* (Fig. 215, left), since it does not occur outside the range of that species. Why this species only should be a capable vector of this disease is unknown; Jellison (1950) suggested that it might be a predilection of *C. discalis* for feeding on rabbits, which constitute an important reservoir of the disease (see pp. 574-575).

Transmission of Other Diseases by Interrupted Feeding. Tabanids may be of importance in transmitting a number of other infectious blood diseases by means of a soiled proboscis during interrupted feeding on herds of animals. Anaplasmosis (see p. 577) can be transmitted

within 5 minutes after feeding on an infected animal. Anthrax can also be transmitted in this manner by either tabanids or *Stomoxys*. This is a very destructive bacterial disease affecting domestic animals and transmissible to man. It may enter the body through skin abrasions, aerial spores, or contaminated food. Since ticks, fleas, and bedbugs have been found capable of transmitting undulant fever or brucellosis, it will not be surprising if tabanids are incriminated also. Tabanids can also transmit swamp fever of horses.

***Loa loa*.** Certain species of *Chrysops*, locally known as mangrove flies, are the intermediate hosts of a human filarial worm, *Loa loa* (see p. 473), in the tropical jungles of Africa. The microfilariae of this worm, unlike those of *Wuchereria bancrofti*, swarm in the blood in the daytime. *Chrysops* is a "pool feeder" (see p. 510), and the number of the large *Loa* microfilariae ingested is very irregular and bears no relation to the number in the circulating blood, in contrast to the fairly regular number of the small *Dipetalonema perstans* embryos ingested from a particular host. Development of the larvae takes place in the abdomen of the fly, but the infective larvae subsequently invade the proboscis as is usual with filariae. The species of *Chrysops* known to be involved are *C. dimidiata* (Fig. 215, right), *C. silacea*, and *C. distinctipennis*. These species are fond of human blood and bite freely in daytime in forest clearings and also attack monkeys in the canopy. They breed along river banks in wet mud covered by thick decaying vegetation in or out of shallow water where there is dense shade (Davey and O'Rourke, 1951).

CONTROL

Cattle can be protected by spraying with a pyrenone emulsion concentrate containing 1 per cent pyrethrins and 10 per cent piperonyl butoxide. Diluted sprays are effective for several days, but light applications, undiluted, are best. Bruce and Davey (1951) devised an apparatus for automatically spraying range cattle as they go through a chute for water or salt, dousing them with one cc. or less of fine spray. Tabanids feeding on them were reduced on the average to less than 1 per cent as compared with control pastures. Dimethyl phthalate as a repellent protects fishermen, etc., for a few hours. In some localities air-spraying of DDT in oil with 1 per cent aluminum stearate at the rate of 1.7 lb. per acre has been used with good effect against the larvae. In Africa the *Loa* vectors may be controlled by clearing brush along stream banks and canalizing stagnant pools, or using larvicides where this is impractical. But—clearing brush might encourage *Anopheles gambiae*, and there would be malaria to contend with instead of *Loa*!

SUBORDER CYCLORRHAPHA

We pass now from the suborder Orthorrhapha to the other suborder of Diptera, the Cyclorrhapha, characterized by the absence of distinct heads in the larvae; escape from the inactive puparium by a circular opening; highly modified wing venation; and highly specialized mouth parts, in some fitted for sucking, in some remodified for piercing after the original piercing organs were lost, and in some entirely vestigial.

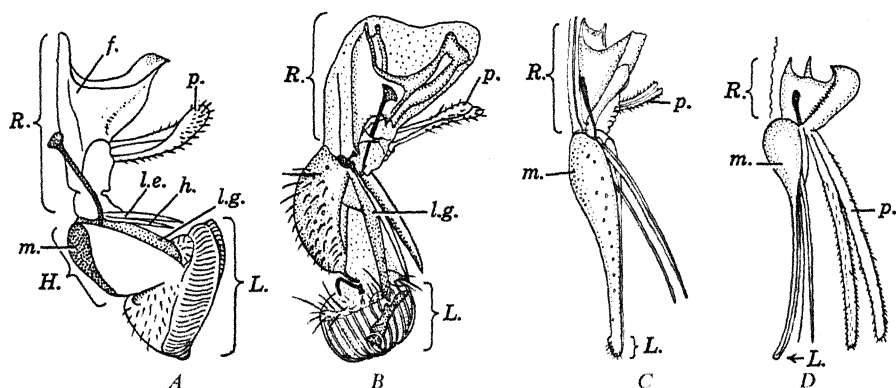


FIG. 216. Evolution of bloodsucking proboscides in muscoid flies. A, *Musca domestica* (for sucking only); B, *Philaetomyia insignis* (for scratching and tearing skin); C, *Stomoxys*, and D, *Glossina*, for piercing. Note progressive shortening of upper segment or rostrum (R); increase in proportionate length of haustellum (H), and increase in chitinized area of it (m); reduction of labellum; freeing of hypostome (h) from labial gutter; development of prestomal armature of spines at tip of labellum; and finally, in *Glossina* (and also in *Pupipara*), elongation and modification of maxillary palpi to form sheath for labium, now the piercing organ. (Adapted from various authors.)

This suborder includes three groups of flies that are important to us: (1) Muscoidea, including some important bloodsuckers, some non-bloodsuckers which are nevertheless important to man or animals as mechanical carriers of disease germs, and a number of species which, like the botflies, are parasitic in the larval stage, causing myiasis; (2) the Pupipara, including important bloodsuckers of animals; and (3) the botflies, which cause various forms of myiasis (see Chapter 30).

The Muscoidea are characterized by having well-developed squamae, normal mouth parts fitted for sucking or piercing, and legs of opposite sides attached close together. Included are the houseflies (Muscidae), stableflies and hornflies (Stomoxysidae), tsetse flies (Glossinidae), and the blowflies, fleshflies, and screwworm flies (Sarcophagidae and Calliphoridae). All were once included in the single family Muscidae.

The majority of the Muscoidea have fleshy proboscides fitted for lapping up liquid foods. Some have acquired the habit of devoting nearly all their time to the skins of animals, flitting from spot to spot in search of blood or exudations. Such, according to Patton (1932), are *M. bezzii* and *M. lusoria*, which are therefore potential mechanical transmitters of blood infections. From these scavengers Patton has traced an interesting evolutionary development of the proboscis into a scratching and tearing and finally a piercing organ (see Fig. 216). *Philaematomyia insignis* (Fig. 216B) is able to rasp and tear a hole through the skin of cattle and suck the exuding fluid. A much higher development is reached in *Stomoxys* and *Siphona* (Fig. 216C), in which the elongated, strengthened, and stylet-like proboscis acts as a piercing organ after a hole has been rasped and torn. The proboscis of the tsetse flies (Fig. 216D) is the culmination in this line of evolution. The tsetse flies and a number of the bloodfeeding species of *Musca* have become viviparous; most of these deposit their larvae at the beginning of the second stage, but one, *M. planiceps*, a bloodsucker, deposits its larvae one at a time at the beginning of the third stage, as do the tsetses.

All the blood-sucking members of the genus *Musca*, all the tsetse flies, and most of the Stomoxyidae are Old World species. Our houseflies, stableflies, and hornflies are probably all importations from across the seas.

Hornflies and Stableflies (Stomoxyidae)

Hornfly (*Siphona irritans*). This small blackish fly, about half the size of a housefly, causes endless misery to cattle; no other pest except possibly screwworms are as inimical to the contentment of cows. The fly sometimes attacks other domestic animals but rarely man. On ranches in the southwest an average of 4000 flies per animal is frequent. They stay on the animals most of the time, night and day, stabbing them and sucking blood usually twice a day. The loss of blood from a herd of 500 cattle with 4000 flies apiece is estimated at 7 quarts a day. The irritated animals become restless, cease to graze, and lose vitality not only from loss of blood but also from loss of food. The resulting heavy loss of meat and milk is inevitable. In 1945 hornflies were estimated to have caused a loss of 86 million pounds of meat in the United States. Fortunately, since they stick fairly closely to one animal, hornflies do not transmit diseases as frequently as stableflies and tabanids.

Hornflies usually leave the animals only to lay eggs. They swarm to a fresh dropping, crawl under it and lay their eggs, and return to the

animal in 5 to 10 minutes. The larvae develop in the dropping in about 10 to 12 days; they are about 7 mm. long and have large black stigmal plates (see p. 743) very close together. They pupate in soil under the dropping; the flat and wingless adults that emerge crawl off to rest for an hour, distending the abdomen and unfolding the wings. The flies live for 6 or 7 weeks and lay about 400 eggs.

Hornflies, because of their habit of staying on animals, are easily controlled by spraying animals with DDT, or preferably Methoxychlor in the case of dairy cattle, since it is not stored internally. One quart of 1 or 2 per cent emulsion per animal followed by 1 pint 3 weeks later is effective. Weight gains quickly follow treatments. Laake estimated that a pound of DDT caused a gain of 2360 lb. of animals. Complete extermination of hornflies might not be extremely difficult unless the flies develop immunity to the chemicals as do houseflies. Unfortunately, however, the day has not yet come when the animals could comfortably dispense with their tails.

Stableflies (*Stomoxys*). The genus *Stomoxys* contains a number of Old World species, but one, *S. calcitrans*, the stablefly or dogfly (Fig. 217), is an annoying pest of animals and man all over the world. In some outbreaks the stablefly may cause as much loss in beef and milk as the hornfly. The stablefly resembles the housefly so closely that it is often mistaken for it, whence the common belief that houseflies can bite. It is easily distinguished by its narrow, pointed, shiny-black proboscis (Figs. 216C, and 217B).

Stableflies breed by preference in decaying straw or rotting vegetable matter or straw mixed with manure, particularly of horses. An unusual scourge of them, sufficient to harass cattle severely and to denude the beaches of bathers, occurs on part of the Florida coast where washed-up piles of seaweed, trapped in lakes behind sand dunes, afford ideal breeding places, especially in September. Later, in December, extensive breeding occurs in piles of peanut litter and celery strippings farther inland.

The eggs are deposited in small batches; in a few days they hatch into white, semitransparent, footless maggots (Fig. 217C) distinguishable by the form and position of the stigmal plates at the posterior end (see Fig. 246). The larvae mature in 10 days to a month or more and pupate in drier parts of the breeding material. The chestnut-colored pupae (Fig. 217D), 6 to 7 mm. long, hatch in a week or more in warm weather.

Stableflies frequently begin a meal on one animal and finish it on another, so they may mechanically transmit diseases such as trypanosomiasis, anthrax, etc., just as do tabanids (see p. 176). They are

particularly important as transmitters of *Trypanosoma evansi*, the cause of surra. *Stomoxys* and *Musca* also serve as intermediate hosts for spiruroid nematodes of the genus *Habronema* (see p. 484), parasites in the stomach of horses. *Habronema* larvae may cause human

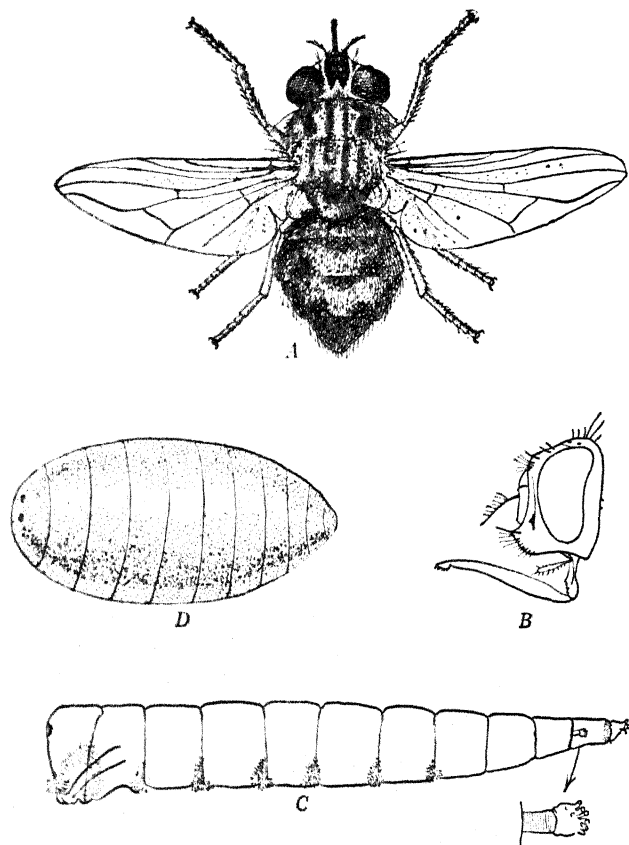


FIG. 217. Stablefly, *Stomoxys calcitrans*. A, adult; B, head, side view; C, larva, with enlargement of anterior spiracle; D, pupa. (Adult, $\times 5$; larva and pupa, $\times 7$.)

conjunctivitis when liberated by flies in the sore eyes of children. *Stomoxys* is also an intermediate host for the filaria, *Setaria cervi*, of deer, and for a tapeworm of chickens, *Hymenolepis carioca*.

In 1912 and 1913 Rosenau and others adduced the theory that the stablefly was responsible for the transmission of poliomyelitis, and the theory was apparently supported by some facts in the epidemi-

ology of the disease (though contradicted by others), and by carefully conducted experiments. In subsequent experiments, however, the results have been uniformly negative. The role of some arthropod is suggested by the epidemiology, but there is little circumstantial evidence against *Stomoxys* (see pp. 232-233).

Where immunity has not developed, control can be obtained by means of sprays on animals or residual sprays in barns (only Methoxychlor or Lindane in dairy barns). The methods recommended for tabanids (p. 670) are also applicable. However, elimination of breeding places is far more feasible than in the case of tabanids. Along the west Florida coast, where marine vegetation washed up on shore breeds enough of these flies to make life miserable, application of 2 gallons of 0.5 per cent DDT emulsion per 100 sq. ft. gave excellent results; about 100 to 600 gallons per mile of shore was needed.

Housefly (*Musca domestica*)

The common housefly, *Musca domestica*, world-wide in distribution, is too well known to require detailed description. About 99 per cent of flies in houses are usually of this species. In the United States the housefly spends *some* of its time creeping over the baby's toys or contemplating the view from a window pane, but in Egypt the variety *vicina* has dedicated itself with an incredible singleness of purpose to crawling over the skin of human beings and driving visitors, at least, frantic. A smaller but related species, *Musca sorbens*, has somewhat different habits; it clusters around the eyes and mouth or sores and sits by the hour, trading germs with its environment. It is also partial to meat in butcher shops, and human feces, which in the Near East may be found practically anywhere, but especially in the animal room of village houses. In many places in the Near East a fly brush for sweeping flies from the face is a most essential piece of equipment and is *one* souvenir a tourist does well to buy.

The housefly is a particularly important transmitter of filth germs, especially those affecting the eyes and the alimentary canal. In Egypt nearly 90 per cent of the village people have trachoma or other eye diseases. When flies were practically eliminated from certain villages by chemicals for a few months, pussy eyes, due to gonococcal infections, were strikingly decreased, although infections due to the "Koch Weeks" bacillus were practically unaffected. The relation to enteric diseases is due to the fact that the fly frequents privies and feces for egg laying, and dining tables and kitchens for food. It harbors vast numbers of germs on its sticky feet; vomits them from its food reservoirs with liquid to melt sugar or cake so that these delicacies will pass

through the pores of its labellum; and deposits germs in its feces (fly-specks). It is probably the greatest single factor in the epidemiology of bacillary dysentery and is an important one in typhoid, cholera, food poisoning, etc. Poultry can become infected with fowl cholera (*Pasteurella*) by feeding on flies that have had access to blood from infected animals. In addition houseflies have been found to pick up and harbor the virus of poliomyelitis, though there is still no evidence that they are an important factor in causing the paralytic form of the disease; their possible role is discussed on pp. 232-233.

The housefly lays its eggs by preference in horse manure but will also use manure of chickens, pigs, or man, and sometimes other decaying animal or vegetable substances, such as that in garbage dumps. The eggs hatch in 12 to 24 hours, and the maggots, recognizable by their stigmal plates (see Fig. 246), are full grown in a few days. They then move to drier places, pupate, and emerge as flies in about 2 to 3 weeks. In her lifetime, averaging about 6 or 8 weeks, a female deposits about 2000 eggs.

The housefly suffered a serious setback when automobiles replaced horses in American cities, and the advent of DDT sprays was thought by many people to spell "finis" for this pest. In fact, *Science News Letter*, in April 1948, carried a big headline "Flyless Age Now in Sight," and some cities and even states seriously set out on campaigns of extermination. Five years earlier this would have seemed a fantastic dream; five years later it is recognized to have been just that. The housefly, to a greater extent than any other insect, has adapted itself to living with DDT, just as it adapted itself to living without horses. After a few months or even weeks a fly population, by natural selection, may become entirely immune (see p. 515). When immunity to one chlorinated hydrocarbon is developed, immunity to others follows more quickly, so *mixtures* of these insecticides should not be used. Also, resistance develops even faster in the larval stage; any chemical used against the adults should not be used against the larvae. A fly population that has become immune to DDT and related chemicals consists of superflies which are hardier in other respects as well, and may become more abundant than in untreated places.

It is obvious that we must return to basic sanitation for fly control—sanitary disposal of feces, frequent thin spreading of manure on farms, burial or burning of garbage or other materials (e.g., at slaughter houses) where flies breed. We must also, for protection against fly-borne diseases, screen houses, protect food on trucks or in shops, etc. It is no easy road, but it is not blocked by impassable barriers as is the attractive-looking road of chemical control.

Blowflies

Although the housefly is the most important mechanical carrier of pathogenic organisms, many other flies may also serve in the same capacity. Attention should be called to the blowflies (Calliphoridae), some of which breed in dung but most of which breed in carcasses. They may carry not only germs of enteric diseases but also those of plague, anthrax, undulant fever, and tularemia. An unsolved enigma, but one that may have significance, is the fact that a high percentage of blowflies (principally *Phoenicia sericata* and *Phormia regina*) collected in the vicinity of poliomyelitis cases were found to harbor the virus. They probably did not get it from human feces; where, then, did they acquire it? The answer might help to solve the problem of polio transmission.

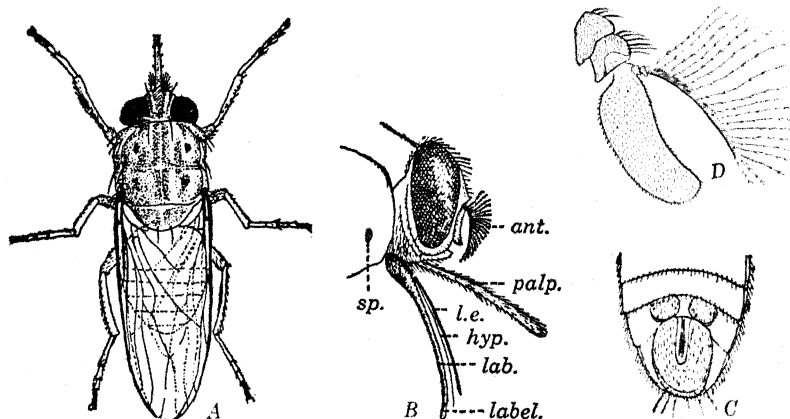


FIG. 218. A, Tsetse fly (*Glossina*) in resting position, $\times 4$ (adapted from Austen and Hegg, *Tsetse Flies*, 1922). B, head and mouth parts; ant., antenna; hyp., hypopharynx; lab., labium; label., labellum; l.e., labrum-epipharynx; palp., labial palpus; sp., spiracle (after Alcock, *Entomology for Medical Officers*, 1920). C, hypopygium of δ , retracted. D, antenna.

Tsetse Flies (*Glossina*)

Tsetse flies are of paramount importance in Africa because of their role as vectors of the trypanosome infections of man and domestic animals, which have had a profound effect on the economy and development of that continent (see p. 152). There are about 20 species of tsetse flies, all belonging to the one genus, *Glossina*, of the family Glossinidae. Except for one species that enters southwest Arabia, the tsetse flies are confined to Africa from south of the Sahara to the northern parts of the Union of South Africa (Fig. 219).

Morphology. The tsetse flies (Fig. 218), are elongated dark brown or yellowish-brown flies, some species no larger than ordinary houseflies, others larger than blowflies. When at rest they fold their wings flat over the back, one on top of the other, instead of spreading them as do most other flies, and the proboscis projects horizontally in front of the head. Even on the wing the darting manner of flight and buzzing sound make them fairly easily recognizable. The appearance of the mouth parts and antennae is characteristic (Fig. 218). The antennae have a conspicuous arista with long feathered bristles on one side only.

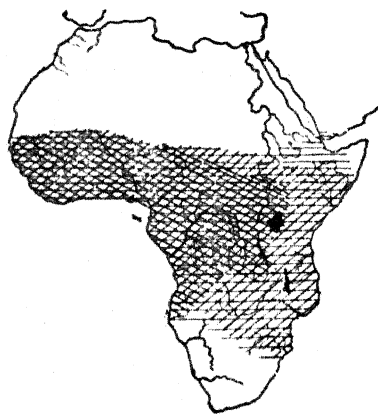


FIG. 219. Approximate ranges of tsetse flies.

- ≡ . . . range of entire genus *Glossina*
 W . . . range of *Glossina palpalis*
 III . . . range of *Glossina morsitans*

The proboscis consists of a piercing labium with a bulb-like base and special structures at its tip for rasping and tearing. In its anterior groove are a delicate labrum-epipharynx forming a food trough and a fine hypopharynx containing the salivary duct. The elongated maxillary palpi, each grooved on its inner face, close together to form a sheath (see p. 671 and Fig. 216D).

The large quadrangular thorax and the tapered abdomen have characteristic patterns in the different species (cf. 221 and 222). In the riverine species (*palpalis* and *tachinoides*), vectors of *Trypanosoma gambiense*, the hind tarsi are all dark, whereas in the *morsitans* group, vectors of *T. rhodesiense* and the animal trypanosomiasis, they are partly pale. Male tsetses have a large oval swelling on the underside of the last segment of the abdomen, the "hypopygium" (Fig. 218C), which forms a good distinguishing mark between the sexes.

Habits. Tsetses are diurnal, although *G. pallidipes* will bite on moonlight nights. *G. tachinoides* stays close to the ground and usually bites below the knee, whereas *palpalis* and others commonly fly 5 or 6 ft. above the ground and more frequently bite above the waist. The usual flight range is only about 500 yards to at most a mile or two, although the flies are often carried considerable distances by vehicles, animals, or bicyclists. Most species avoid either thick underbrush or park-like areas under a canopy, since they commonly rest on the underside of twigs near the ground, and deposit their young under low

shade. *G. tachinoides* is entirely barred by thick underbrush, and even the *morsitans* group avoids dense unbroken thickets. Most species can stand considerable ranges of climate and environment. *G. palpalis* and *tachinoides* are found only close to water along rivers or lake shores except in wet rain-forests; *palpalis* seldom thrives where there is less than 45 in. of rain, but *tachinoides* may extend along rivers to a 15 in. zone. The *morsitans* group, on the other hand, is partial to savannah-woodland, frequenting clumps or stretches of certain types of vegetation surrounded or interspersed by open grassland, into which the flies make hunting forays to feed on game animals. Moving objects or even large quiet objects attract them, so small clearings for distances of only 100 yd. or so along streams may increase rather than decrease fly-man contacts. Tsetses show marked preference for certain colors; the dark skin of Negroes is selected in preference to pale skin to such an extent that a white man is seldom troubled when accompanied by natives.

Both sexes of tsetse flies are bloodsuckers, but they also suck plant juices. Different species have different tastes. The *G. morsitans* group, including *pallidipes* and *swynnertoni*, feed mainly on large mammals (game animals) and are unable to keep going in their absence. These are the most important transmitters of *T. rhodesiense* of man and of the animal trypanosomes—*brucei*, *congolense*, and *vivax*, and their relatives—which are so deadly to domestic animals that in the presence of these flies it is impossible to keep anything but poultry and a few fly-hardened goats. Small mammals are of little use to these or other tsetses because of their retiring and nocturnal habits. It is a case of game and tsetses or man and cattle—it can't be both. The riverine species of tsetses (*G. palpalis* and *G. tachinoides*) which transmit *T. gambiense* to man, on the other hand, are able to thrive where there is no game and man is the only source of food, except for occasional blood meals supplied in a pinch by lizards, crocodiles, or birds.

Life History. Tsetse flies differ from most related flies in their remarkable manner of reproduction. They do not lay eggs; a single developing larva is retained within the body, being nourished by special "milk glands" on the walls of the uterus while lying with its stigmal plates, containing the spiracles, close to the genital opening of the mother. The larva passes through its molts and is full grown and ready to pupate before it is born, occupying practically all of the swollen abdomen of the mother. As soon as one is born another begins its development, and new larvae are born about every 10 or 12 days, provided that the temperature is around 75° to 85°F. and food is abundant. There are few data on the total number of young produced, but in one captive fly eight larvae were produced in 13 weeks, and only one egg

was found left in the body. Pregnant flies often abort when disturbed, and cases are known in which the larvae pupated within the abdomen of the mother, to the destruction of both of them. Breeding occurs mainly in the dry season.

The larva (Fig. 220C) is a yellowish-white creature about 8 to 10 mm. in length, with a pair of dark knob-like protuberances at the posterior end, between which are the stigmal plates. Immediately after birth it hides itself at a depth of 1 to 2 cm. in loose soil or under dead leaves and transforms to a pupa (Fig. 220D). This is olive

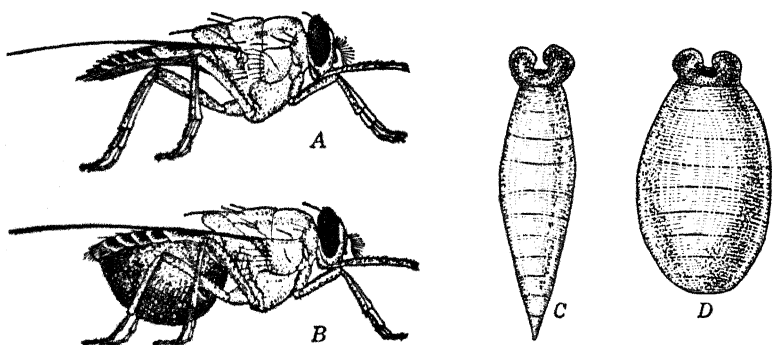


FIG. 220. A and B, *Glossina morsitans* before and after feeding, $\times 4$ (adapted from Austen and Hegh, *Tsetse Flies*, 1922). C, newly born larva of *G. palpalis*. D, pupa of *G. palpalis*.

shaped, and turns a mahogany color, with the blackish knobs still present at the posterior end; the shape and size of these knobs and of the notch between them are useful species characters. The duration of the pupal stage may be 17 days to nearly 3 months. Few adults emerge at temperatures below 70° or above 86°F .

All species select dry, loose soil in shaded, protected spots for deposition of the grown larvae. As maternity spots, *G. morsitans* and its allies select places under logs, hollows under trees, etc., whereas *palpalis*, less resistant to unfavorable temperature and humidity, gives birth to its young in sites protected by low as well as high shade; *tachinoides*, except in more austere parts of its range, needs only high shade.

Adult tsetse flies apparently live for only a few months in the wet season, and possibly for only about 3 weeks under dry conditions. In the drier parts of their range *palpalis* and *tachinoides* often concentrate in the vicinity of a few persisting water holes along the course of a stream. Since the human population does likewise, it is obvious that even though the flies may not be numerous, the contacts with man are numerous,

and conditions are ideal for transmission of human trypanosomiasis (see p. 163). The infected people, frightened by outbreaks of the disease, or seeking new water holes, or migrating along trade routes, spread the disease further. There is one record of 30 of 43 people in a hamlet becoming infected, the source being a small water hole where four tsetse flies did the job. In wet coastal areas, even though the flies may be far more numerous, they are more dispersed, have more alternative sources of food, and there is much less sleeping sickness.

TSETSE FLIES AND TRYPANOSOMIASIS

The principal transmitters of *Trypanosoma gambiense* of man are *Glossina palpalis* and *G. tachinoides*; in parts of northern Nigeria and northern Cameroons *G. tachinoides* is the primary transmitter. The principal transmitter of *T. rhodesiense* of man is *G. morsitans*, although in some areas in East Africa the related *swynnertoni* and *pallidipes* are equally or more important; in an epidemic in Uganda in 1940-1943 *pallidipes* was the principal vector. This *morsitans* group, as remarked above, includes the principal species concerned in transmitting the animal trypanosomes, even in places where *palpalis* and *tachinoides* are commoner. In parts of West Africa *longipalpis* is another important vector to animals, and in East Africa *brevipalpis*. Other species, either because of their rarity or their food habits, are less important. The *morsitans* group is also able to transmit *T. gambiae* experimentally, but its dependence on game results in its being scarce except where there are few human beings (less than 40 per square mile). The importance of this group of flies in transmitting *rhodesiense* to man is undoubtedly due to this species of trypanosome utilizing wild game as a reservoir to a much greater extent than does *T. gambiense*. As noted in Chapter 8, even in many places where 20 or 30 per cent of game harbor trypanosomes only a small percentage of the flies may be infected. Some strains of flies seem more refractory than others.

Glossina palpalis (Fig. 221) is a large dark species with blackish-brown abdomen, and gray thorax with indistinct brown markings. Its wide distribution in west and central Africa, shown in Fig. 219, is nearly coincident with that of Gambian sleeping sickness. In the rainy season the flies may extend their range and retreat again as the water dries. This species is seldom found more than 30 yd. from the edge of a river or lake where vegetation overhanging the water is abundant, although it follows man or animals for a few hundred yards from such positions. It is feared that *G. palpalis* may sometime bridge the short gap between the headwaters of the Congo and the Zambesi and become

established along the latter river and its tributaries, carrying sleeping sickness with it.

G. tachinoides is one of the smallest tsetse flies, about the size of a housefly, occurring around the southern border of the Sahara. It has habitats similar to those of *palpalis*, but it is able to live in more sparsely shaded places with less rainfall, and it is absent from the wet coastal areas. It feeds on animals primarily but is not entirely dependent on game. It is an important vector of sleeping sickness only in sacred groves, around water holes, etc., where there is little choice of hosts and contact with man is close.

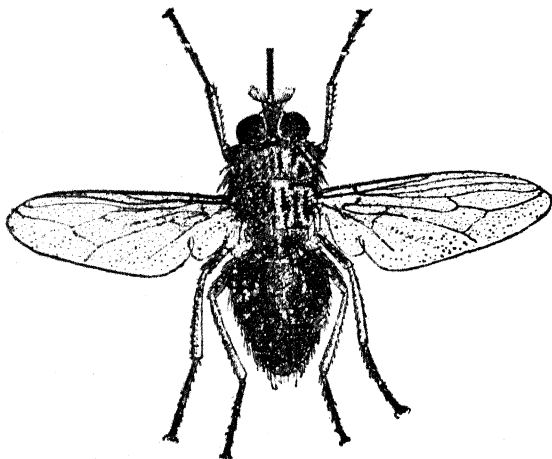


FIG. 221. *Glossina palpalis*, carrier of Gambian and Nigerian sleeping sickness. $\times 4$. (After Austen and Hegg, *Tsetse Flies*, 1922.)

G. morsitans (Fig. 222) is the most widely distributed species of tsetse fly (see Fig. 219) and is also the best known, having attracted the attention of big-game hunters in Africa for many years. It is slightly smaller and much lighter colored than *G. palpalis*, with distinctly banded abdomen. *G. morsitans* is not confined to the immediate vicinity of water. It prefers dry savannahs interspersed with patches of bush or woodland where there is a moderate amount of shade, but shows strong predilections for certain types of vegetation. It is not found in open grassland or in deep forest. A thin, deciduous woodland called "miombo" is an especially favored habitat, but within any environment this and other species exercise a very precise choice of places to feed, rest, or breed. With sufficient knowledge tsetses can sometimes be eliminated by surprisingly little "discriminative" clearing in local areas.

G. swynnertoni favors somewhat drier and sparser vegetation than does *morsitans*, whereas *pallidipes* and *brevipalpis* favor somewhat greater humidity and denser thickets. All these species are closely related and are good trypanosome transmitters.

CONTROL

G. palpalis and *G. tachinoides*, which live along rivers and shores of lakes, are easier to control than the *morsitans* group, which is independent of water. Partial clearing along river banks by elimination of brush and low branches of trees, with "ruthless" (complete) clearing

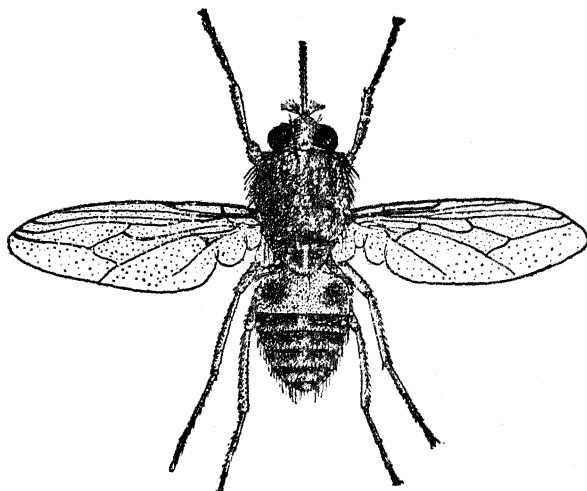


FIG. 222. *Glossina morsitans*, carrier of Rhodesian sleeping sickness. $\times 4$. (After Austen and Hegh, *Tsetse Flies*, 1922.)

for a mile at the ends of the cleared areas to prevent reinfestation in wet seasons, will eliminate these species from sections of stream or even whole river systems. This has been demonstrated in Nigeria and the Gold Coast. To reduce contacts between fly and man and thus reduce human trypanosomiasis, "defensive" clearing is done on either side of villages, bridges, fords, etc. Clearings for less than 200 yards *increases* man-fly contacts by making man more visible. Ruthless clearings of 500 to 800 yards reduce FBH (flies per boy hour) 60 per cent. Clearings of 800 to 1000 yards give the highest rate of freedom from flies that is economically practicable. For these flies game extermination or exclusion is useless.

Control of the *morsitans* group is more difficult. In earlier days

the only solution when sleeping sickness outbreaks occurred was to relinquish the land to the tsetse and game, and move the human population to less dangerous places. This is sometimes still the best policy where the land is poor and population sparse. Now, however, in areas that are worth it, the land *can* be reclaimed for man and domestic animals and the tsetse banished. The methods used include (1) direct attacks on the flies by insecticides, traps, burning, etc., (2) game destruction or exclusion, (3) clearing of certain types of vegetation, and (4) human settlement.

Only *complete* elimination is adequate, but 95 to 99 per cent control has sometimes been given by DDT applications over large areas by air, or locally by spraying cattle or bicyclists' clothes and then having them pass back and forth through an area; generating DDT smoke; using traps of various kinds; burning breeding areas; etc.

Destruction of game is a successful method on more or less isolated areas of a few hundred square miles, but one which is often looked upon with considerable repugnance. It is, however, a choice between preserving the game for hunters and naturalists or making land available for development by man. Game reserves in areas unsuitable for development—and there are plenty of them—will prevent extermination of the animals. Danger that with game destruction the tsetse will turn their attention to domestic animals is remote, for as Buxton (1948) pointed out there is no moment when numerous hungry flies could do this. Until all the game is gone, and the tsetse with it, there are not yet any domestic animals available. Fencing of various types has been tried, but the expense and difficulties involved rarely make it feasible. It was primarily by game destruction that over 6000 square miles in Southern Rhodesia have been reclaimed from tsetse for use of man and animals.

Reclamation by "discriminative" clearing of vegetation favored by flies has been successful in over 1300 square miles in Tanganyika. Methods include late burning, felling, and bulldozing, with help from cultivation and browsing goats. With increasing knowledge of the fly's predilections, successful clearing becomes less difficult, but much is yet to be learned.

Human settlement can hold land that has been cleared of tsetse and makes advances into a fly belt possible; the game and tsetse abandon more and more land instead of *man* doing this. However, there are problems. Most of the land to be reclaimed is marginal, and if enough settlers occupy it to drive off the game, the land is overstocked or overworked and starvation eventually replaces trypanosomiasis. There is clearly no easy road to the development of Africa unless the use of

prophylactic drugs in animals and man may bring about a partial solution (see pp. 165-166, 177).

Eye Flies (Chloropidae)

The eye flies (Fig. 223) are small, nearly hairless flies, about 1.5 to 2.5 mm. long, of the family Chloropidae (or Oscinidae). The larvae of some species are pests of growing wheat, etc., but most of those

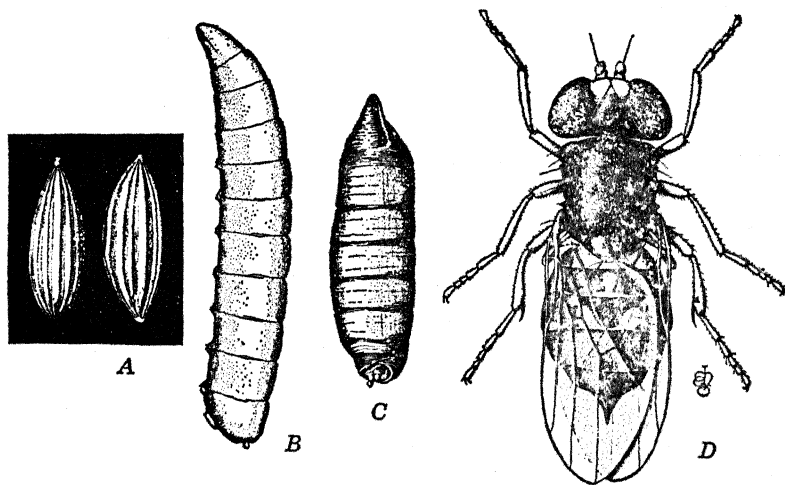


FIG. 223. Stages in life cycle of California eye fly, *Hippelates collusor*. A, eggs, in dorsal and lateral views; B, mature larva; C, pupa; D, adult ♀. A, about $\times 45$; B, C, and D, about $\times 18$. (After D. G. Hall, *Am. J. Hyg.*, 16, 1932.)

annoying to man breed in excrement or decaying organic matter. *Hippelates collusor* (so called by Sabrosky; usually called *pusio*, a common southeastern species) was found by Hall to breed in almost any substance in an advanced state of decay, but when artificially bred it did best in human excrement.

According to Hall the entire development from egg to adult required 11 days or more, averaging about 18 days, but Burgess (1951) found 28 days to be required and thought in nature the time might be extended to several months or nearly a year. Although the eye flies are not bloodsuckers in the ordinary sense, many of them are habitually attracted by the skin and natural orifices of man and animals, lapping up perspiration, excretions, exudations of sores and wounds, or blood from scratches or insect bites. Some species appear to be especially attracted to the eyes and lachrymal secretions of man, whence their

name. The proboscis is fitted for lapping, as in the housefly, but is capable of being used as a rasping instrument to cause minute scarifications on the delicate conjunctival epithelium or on granulation tissue of sores, thus assisting pathogenic organisms in gaining entrance. The habits of these insects, therefore, render them particularly dangerous mechanical carriers of eye infections and of various diseases of the skin and mucous membranes as well. Graham-Smith (1930) gives a review of the principal species concerned in disease transmission.

Relation to Eye Diseases. In the Coachella Valley of California *Hippelates collusor* (Fig. 223), and in parts of Florida *H. pusio*, are a sufficient nuisance to be limiting factors in the development of the country. They are small flies, 2 mm. in length, which are active throughout the day for 9 or 10 months of the year, but particularly in spring and fall. They persistently buzz around the heads of men and animals, frequently darting at the eyes or into the ears or feeding on sores or mucous membranes. In one high school 1500 children were reported as suffering from "pinkeye" in 1929; 50 per cent of the young children of the region had some conjunctivitis, and 10 per cent had chronic trachoma.

In India and the East Indies another member of the family, *Siphunculina funicola*, with similar habits, is responsible for spreading conjunctivitis and probably skin infections also. In Egypt, where eye infections are particularly common, houseflies and related species are usually considered to be the principal transmitting agents, but chloropid flies are very common in some places and should be investigated in connection with the ophthalmia that is so prevalent.

Eye Flies and Yaws. Members of the family Choropidae are an important, perhaps one of the most important, factors in the transmission of yaws (see pp. 68-69). Nichols in 1912 was convinced that eye flies, *Hippelates flavipes*, were responsible for the majority of cases of yaws in the West Indies, and similar views have been expressed by a number of other writers in the West Indies and Brazil. In Trinidad this species is called the "yaws fly."

Kumm and Turner (1936) found that the spirochetes of yaws remain motile in the pharynx and esophageal diverticula of *H. flavipes* for at least 7 hours but lose their motility in the midgut and do not undergo development in the fly as do the spirochetes of relapsing fever in lice. The flies commonly regurgitate drops of fluid after feeding; these drops contain viable spirochetes. Kumm and Turner experimentally transmitted the disease to rabbits both by bites of the flies and by inoculation of esophageal diverticula. There is a close correlation between the distribution of this fly and that of yaws in the West Indies.

It was possible to catch over 1500 flies feeding on yaws sores within 15 minutes, so the opportunities for transmission are obvious.

In Assam, Fox in 1921 showed that epidemics of another spirochetal infection, Naga sore (see p. 71), are associated with plagues of *Siphunculina funicola*, which swarm on the sores and mechanically transmit the infective material.

Control. Control of these flies is difficult, but the suppression or treatment of decaying organic matter and improved sanitation to prevent breeding in human excrement would be of some value. Parman in 1932 advocated the use of box traps baited with odoriferous decaying infusions. DDT spraying of animals for other flies, and of buildings, etc., for houseflies, will certainly reduce the number of eye flies.

Pupipara

This peculiar group of Diptera, sometimes called louse flies, ectoparasites of birds and mammals, have leathery, sac-like abdomens and have the opposite legs inserted wide apart. The mouth parts are similar to

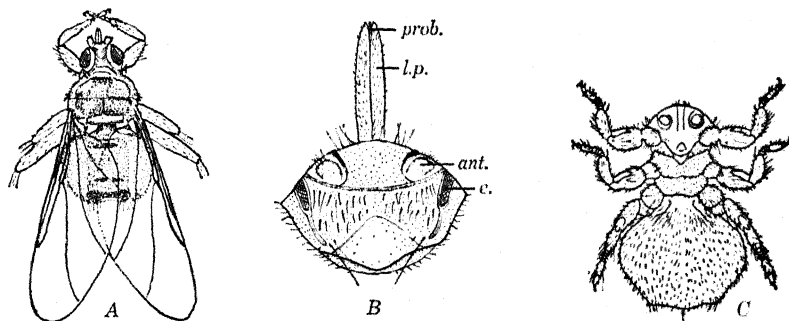


FIG. 224. A, *Pseudolynchia canariensis*; note large eyes and exposed antennae; B and C, *Melophagus ovinus*, the ked or "sheep tick." In B, note small eyes, antennae sunk in pits, and long palpi sheathing mouth parts, as in tsetse flies. (A and B adapted from Massonat, *Ann. Univ. Lyon*, 1909. C from Metcalf and Metcalf, *A Key to the Principal Orders and Families of Insects*, 1928.)

those of a tsetse fly but with the piercing proboscis partly retractile into a pouch in the ventral part of the head, the projecting part then sheathed by the labial palpi. In the winged forms the eyes are large and the antennae exposed, but in the wingless "sheep tick," *Melophagus ovinus*, the eyes are small and the reduced antennae sunken in pits on top of the head (Fig. 224B, C). As the name Pupipara implies, they give birth, one at a time, to larvae which are fully mature and ready to pupate. In most species the larvae are deposited in dry soil or humus, in the nests of birds, or in other protected spots where

they transform at once into pupae and turn a shiny black. In the subfamily Melophaginae, however, the motionless larvae are deposited in the wool or fur of the host; the wingless ked or "sheeptick," *Melophagus ovinus*, has the larval skin covered by a glue-like substance which sticks it to the wool, whereas the pupae of *Lipoptena*, parasitic on deer, mostly fall out of the fur in wallows when the deer shed their winter coat. These undergo a diapause (cessation of development) until fall, when the winged adults emerge and seek a new host, soon after which the wings break off.

There are two families of un-fly-like Pupipara parasitic on bats ("bat ticks") and one family on bees. Those parasitic on mammals and birds belong to the family Hippoboscidae. The genus *Hippobosca* includes winged forms parasitic on horses, cattle, camels, dogs, etc., in the Old World. *Pseudolynchia*, also winged, attacks nestling birds; one species, *P. canariensis* (= *maura*) (Fig. 224A), is the intermediate host of the common pigeon parasite, *Haemoproteus columbae* (see p. 184). *Lynchia fusca* transmits *H. lophortyx* among California quail. The ked or "sheeptick," *Melophagus ovinus* (Fig. 224B, C), mentioned above, is annoying to sheep, and may do severe harm to poorly nourished ones. The females give birth to a full-grown larva every 7 or 8 days until a total of 12 or 15 have been born. The pupal stage lasts for about three weeks, and the adult is ready to be a mother about 2 weeks after emergence. The ked serves as an intermediate host for the non-pathogenic *Trypanosoma melophagium* of sheep, and it also harbors a rickettsia.

The Pupipara only exceptionally bite man but produce painful bites when they do so.

Keds are easily controlled by DDT, rotenone, or other sprays applied under pressure, or by dips or even dusts. The pupae are not killed, but the residual effect lasts long enough to kill the adults when they emerge.

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• 29 •

Diptera

II. Mosquitoes

Importance. Of all existing insect pests mosquitoes are Public Enemy No. 1. The mere annoyance which the enormous numbers of them cause by their bites is sufficient to have made some parts of the world practically uninhabitable. Rich pieces of country have remained unsettled and some of the choicest hunting and camping grounds in North America are practically closed to the camper by the countless millions of mosquitoes that transform a camper's paradise into an intolerable hell. Unlike most insect pests the mosquitoes in the Far North are more abundant than they are in the tropics. In places in Alaska mosquitoes have been observed to land on the back of a woolen glove at the rate of 70 per minute, and spray equipment for outdoor insect control is as necessary to the civilized life of residents as are roads or a kitchen stove.

Fortunately these far northern mosquitoes are not disease transmitters, whereas many tropical mosquitoes have their spears poisoned with death-dealing disease germs. No less than four important human diseases are normally transmitted by mosquitoes exclusively—malaria, yellow fever, dengue, and filariasis. In addition, various forms of encephalomyelitis (see p. 233) are primarily transmitted by mosquitoes, and a South American fly, *Dermatobia*, usually depends on mosquitoes for transportation of its eggs to the skin of man or animals, where they hatch and cause myiasis. Fowlpox of poultry, fibroma of rabbits, and numerous forms of bird malaria are also transmitted by mosquitoes.

General Structure. Mosquitoes, comprising the family Culicidae (see key, p. 646), can easily be distinguished from all other Diptera, some of which superficially resemble them, by the presence of scales along the wing veins and a conspicuous fringe of scales along the hind margin of the wings. The venation (see Figs. 152 and 233) is very similar in all the species, but the coloration produced by the scales, especially in *Anopheles*, is useful in identification of species in that genus. Most of the Culicidae have a long prominent proboscis con-

taining needle-like organs for piercing and sucking, but in one sub-family there is no long proboscis.

Figures 225, 226, 227, 228 and 233 illustrate the main features of a mosquito. The sexes can be distinguished most readily by the antennae (Fig. 226); in the female they are long and slender with a whorl of a few short hairs at each joint, whereas in the male they have a feathery appearance due to tufts of long and numerous hairs at the

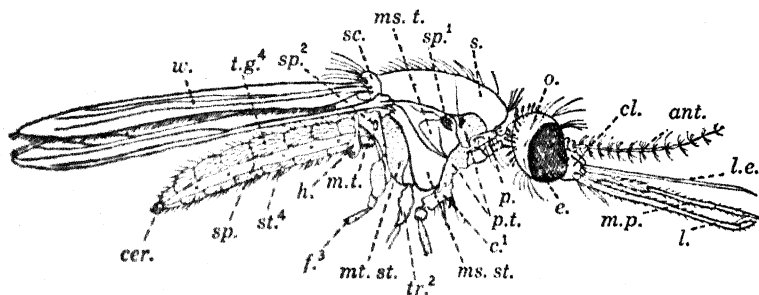


FIG. 225. Diagram of mosquito, showing parts of body. The prothorax and metathorax with their respective legs are stippled, the mesothorax not stippled: *ant.*, antenna; *c.*, coxa of first leg; *cer.*, cerci; *cl.*, clypeus; *e.*, eye; *f.*, femur of the third leg; *h.*, haltere; *l.*, labium; *l.e.*, labrum-epipharynx; *m.p.*, maxillary palpus; *ms.t.*, mesosternum; *ms.t.*, mesothorax; *mt.st.*, metasternum; *m.t.*, metathorax; *o.*, occiput; *p.*, palpi; *p.t.*, prothorax; *s.*, scutum; *sc.*, scutellum; *sp.*, abdominal spiracle; *sp.*¹ and *sp.*², first and second thoracic spiracles; *st.*⁴, sternite of fourth abdominal segment; *tg.*⁴, tergum of fourth abdominal segment; *tr.*², trochanter of second leg; *w.*, wing. (After Nuttall and Shipley, from Hindle, *Flies and Disease. Bloodsucking Flies*, 1914.)

joints. In many mosquitoes the palpi also furnish a means of distinguishing the sexes; they are usually long in the males but short in the females (Fig. 226), but in *Anopheles* they are long in both sexes, and in some mosquitoes, e.g., *Uranotaenia*, they are short in both.

The proboscis also differs in the sexes and fortunately is so constructed in the male that a mosquito of this sex could not pierce flesh if he wished. At first glance the proboscis appears to be a simple bristle, sometimes curved, but when dissected and examined with a microscope it is found to consist of a number of needle-like organs lying in a groove in the fleshy labium which was the only part visible before dissection. In the female mosquito there are six of these needle-like organs, the nature and names of which are shown in Fig. 227. The labrum-epipharynx and hypopharynx act together to form a tube for drawing up blood into the mouth. A tiny tube runs down through the hypopharynx, opening at its tip, through which saliva is poured into the wound as through a hypodermic needle to prevent blood from coagulating. The maxillae and mandibles are needle-like piercing organs,

the former recognizable by their sawtooth tips. The ensheathing labium bows back at the mosquito bites, the flexible tip or labellum acting as a guide for the piercing organs as they are sunk into the flesh. In male mosquitoes the piercing organs are much degenerated, only the suctorial part of the apparatus being well developed.

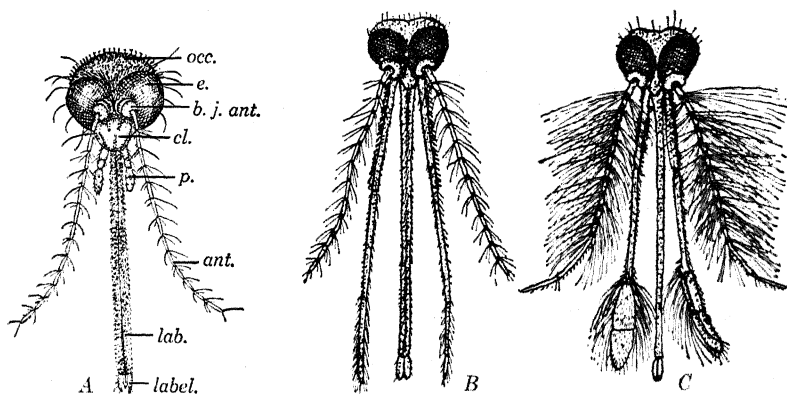


FIG. 226. Heads of mosquitoes. A, ♀ *Culex*; B, ♀ *Anopheles*; C, ♂ *Anopheles*; ant., antenna; b.j.ant., basal joint of antenna; cl., clypeus; e., eye; lab., labium; label., labellum; p., palpus; occ., occiput.

Besides the variations of the parts mentioned already, adult mosquitoes vary in the form, distribution, and color of the scales that clothe much of the body and the edges and veins of the wings; the distribu-

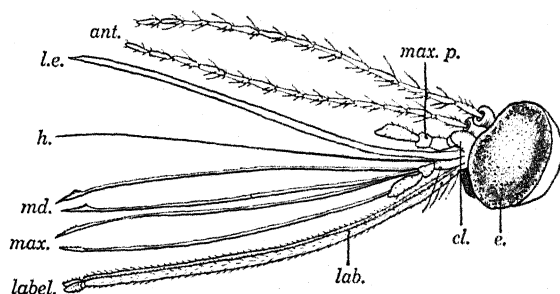


FIG. 227. Head and mouth parts of ♀ culicine: ant., antenna; cl., clypeus; e., eye; h., hypopharynx; lab., labium; label., labellum; l.e., labrum-epipharynx; max., maxilla; max.p., maxillary palpus; md., mandible. (After Matheson, *Medical Entomology*, Comstock.)

tion of bristles on the thoracic sclerites (Fig. 233); the details of the male reproductive organs at the tip of the abdomen (Fig. 228); the details of the female hypopygium; the relative length of parts of the leg; and in other respects. Mosquitoes have three food reservoirs

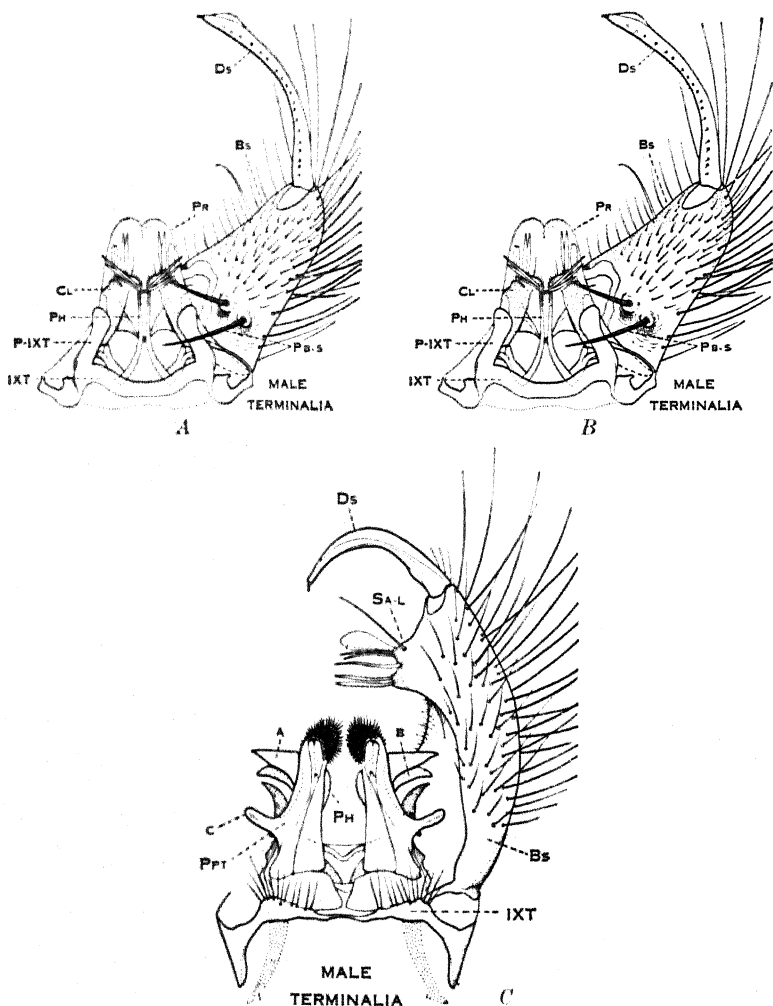


FIG. 228. Male genitalis of mosquitoes. A, *Anopheles quadrimaculatus*; B, *Aedes aegypti*; C, *Culex fatigans*. Abbreviations: *b.s.*, basistyle or side piece; *cl.*, claspette, with spines; *d.s.*, dististyle or clasper; *ph.*, phallosome or aedeagus; *pr.*, proctiger or anal lobe; *sal.*, subapical lobe (only in *Culex*). (After Ross and Roberts in *Mosquito Atlas*, 1.)

connected with the esophagus, in addition to a large stomach (Fig. 46). These reservoirs are used for storage of "aspirated" foods such as fruit juices, but not for blood, which passes directly to the stomach. This reduces the probability of *direct* transmission of disease germs immediately after an infective feed. Connected with the proboscis

is a pair of salivary glands consisting of three lobes each, lying in the anterior part of the thorax. It is in these that the malaria parasites collect after development; from here they are poured with the secretions of the glands into the wounds.

Life History and Habits

In a general way the life histories of all mosquitoes are much alike, but they differ in details.

Eggs. The eggs of mosquitoes (Fig. 229) are usually oval with various surface markings and, in *Anopheles*, with a peculiar "float" of air cells. The number of eggs laid by one female mosquito varies

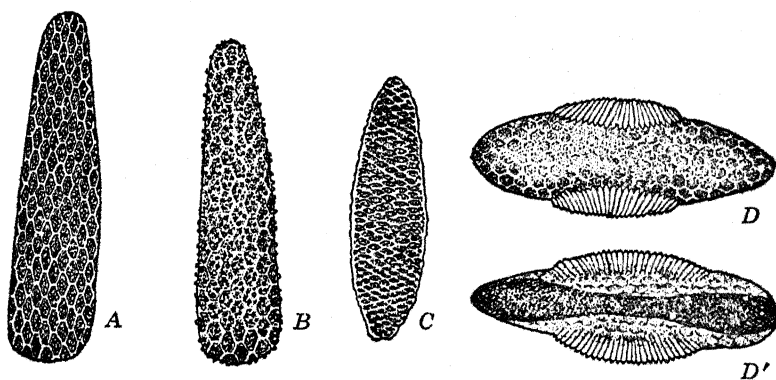


FIG. 229. Eggs of mosquitoes: A, *Theobaldia inornatus*; B, *Mansonia perturbans*; C, *Aedes aegypti*; D, *Anopheles punctipennis*, dorsal view; D', same, ventral view. $\times 75$. (After Howard, Dyar, and Knab, *Carnegie Inst. Wash. Publ.* 159, 1912-1917.)

from 40 or 50 to several hundred. Species of *Aedes* and *Psorophora* lay their eggs singly out of water; *Anopheles* lays them singly in loose clusters on water (Fig. 230A); *Culex*, *Theobaldia*, and *Uranotaenia* lay them in little boat-shaped rafts called egg-boats, the individual eggs standing upright (Fig. 230B); and *Mansonia* lays them in irregular clusters on the underside of floating leaves.

Species of *Anopheles*, *Culex*, *Theobaldia*, and *Mansonia*, which are common in warm climates, lay their eggs on the open surface of water or attach them to some partially submerged object. Species of *Aedes* and *Psorophora*, on the other hand, lay their eggs out of water in places likely to be submerged later, e.g., in dry depressions in the North that will be filled with melted snow the following spring, in dry depressions in marshes or meadows that will be flooded after rains or high tides, or just above the water line in tree holes or containers. This

is a useful biological adaptation to make an adequate supply of water likely when the eggs hatch.

When the eggs are laid on water they may hatch in a few days, or even within 24 hours, but those laid out of water lie unhatched until submerged, which may be weeks or months, and even then only a fraction of them usually hatch at the first immersion. The eggs of the far northern species are said not to hatch unless they have been exposed to freezing temperatures. Mosquitoes of dry, hot countries lay eggs that are highly resistant to desiccation and do not lose their vitality during months of dryness. Such species must almost "live while the

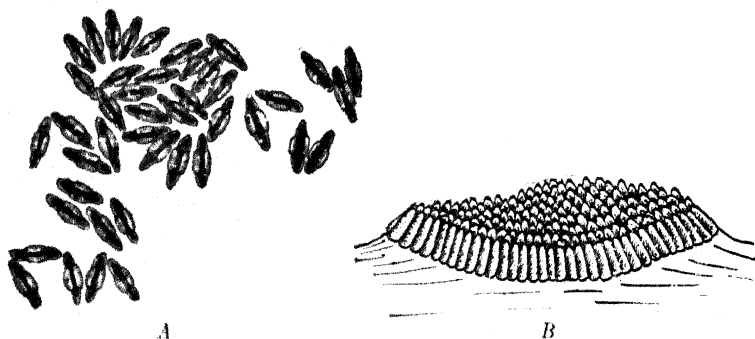


FIG. 230. Eggs of mosquitoes: A, eggs of *Anopheles* on surface of water, $\times 13$ (after Howard, *Farmer's Bull.* 155, 1908). B, egg-boat of *Culex* floating on water, about $\times 6$.

rain falls" and must be prepared to utilize the most transitory pools for the completion of their aquatic immature stages. In such cases the embryo within the egg shell develops to the hatching point, so that it is ready to begin the larval existence almost with the first drop of rain. Eggs of some species of *Aedes* (*vexans* and *lateralis*) may remain viable in the soil for several years.

Such mosquitoes further fortify their race against the unkind environment by laying their eggs in a number of small batches instead of in a single mass, as is the habit of mosquitoes where water is plentiful. Just as a man runs less risk of ruin if he deposits his money in a number of insecure banks rather than in a single uncertain one, so it is with mosquitoes and the places where they deposit their eggs. The failure of all of a batch of dried eggs to hatch at any one immersion is a similar adaptation.

The vagaries of different species in selecting breeding places are discussed on the following pages. The only feature common to all is the fact that the eggs do not hatch except in the presence of water.

Larvae. The larvae, which are always aquatic, are well known as wrigglers or wiggle-tails (Fig. 231). When first hatched they are almost microscopic, but they grow rapidly to a length of 8 to 15 or 20 mm. The bunches of long bristly hairs on the body take the place

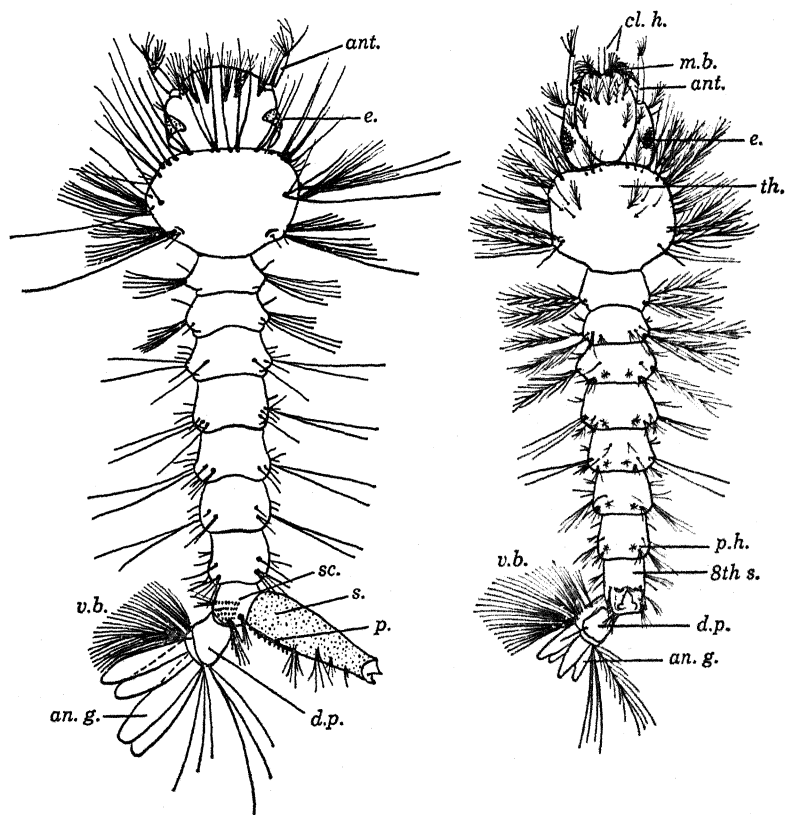


FIG. 231. A, Larva of *Culex fatigans* (after Soper); B, larva of *Anopheles punctipennis* (after Matheson); an.g., anal gills; ant., antenna; cl.h., clypeal hairs; d.p., dorsal plate of 9th segment; 8th s., 8th segment of abdomen; e., eye; m.b., mouth brush; p., pecten; p.h., palmate hair; s., siphon or breathing tube; sc., patch of scales on 8th segment; th., thorax; v.b., ventral brush.

of legs and aid the larva in maintaining a position in the water. There is a rotary mouth brush of stiff hairs used to sweep small objects toward the mouth; in predaceous species these are sometimes modified into rake-like structures or into strong grasping hooks for holding prey (Fig. 235, 8).

A trumpet-shaped siphon or breathing tube is present on all mosquito larvae except *Anopheles*, in which it is undeveloped. It is used to

pierce the surface film of the water to draw air into the tracheae for, although aquatic, mosquito larvae are air breathers and make frequent trips to the surface to replenish their air supply. The leaf-like anal gills on the last segment of the abdomen differ from true gills in that air tubes or tracheae instead of blood vessels ramify in them. They may function primarily as osmotic regulators rather than respiratory organs since they are always larger in mosquitoes living in saline water. In well-aerated water larvae can live for a long time, but they die within a few hours if shut in water without dissolved air. In one genus, *Mansonia*, the larvae absorb air from the air-carrying tissues in the roots of certain aquatic plants, piercing them with the apex of the breathing tube (Fig. 235. 11) and thus avoiding the necessity of rising to the surface of the water.

Mosquito larvae, unless suspended from the surface film by means of the breathing tube, have a tendency to sink, and they rise again only by an active jerking of the abdomen, using it as a sculling organ. Some species are habitual bottom feeders; others feed at the surface; some live on microscopic organisms, others on dead organic matter; and still others attack and devour other aquatic animals, including young mosquito larvae of their own and other species. Soluble and colloidal substances in water can also be utilized.

The larvae shed their skins four times and then go into the pupal stage. Mosquitoes of temperate climates usually take 5 days to 2 weeks to complete the larval existence, depending almost entirely on temperature and abundance of food. In the mosquitoes adapted to take advantage of transitory rain pools the larvae may transform into pupae within 2 days. On the other hand, some mosquitoes habitually pass the winter as larvae. Larvae of most mosquitoes can live for several days on a wet surface but do not succeed in pupating except in water. Adults usually succeed in emerging from pupae stranded on mud.

A key for the identification of the larvae of different genera, and of important American species, is given on pp. 708-711.

Pupae. The general form of the pupa can be seen in Fig. 232; it resembles a tiny lobster deprived of appendages and carrying its tail bent. The pair of ear-like breathing tubes on the cephalothorax takes the place of the trumpet-like tube of the larva and is used in the same manner. Unlike the larva, the pupa is lighter than water and requires muscular effort to sink instead of to rise. The pupae of *Mansonia*, like the larvae, do not come to the surface for air but pierce the air channels in the roots of aquatic plants with their pointed breathing tubes.

The transformation into the adult during the pupal stage may be a matter of a few hours in the case of the dry-climate mosquitoes, but in most species it requires 2 days to a week, depending on the temperature. The adult mosquitoes emerge head first through a longitudinal slit along the back of the thorax. After their exit they rest a few moments on the old pupal skin, stretch and dry their wings, and then take flight. They may suck blood within 24 hours, but several days to a week or more elapse before they lay eggs.

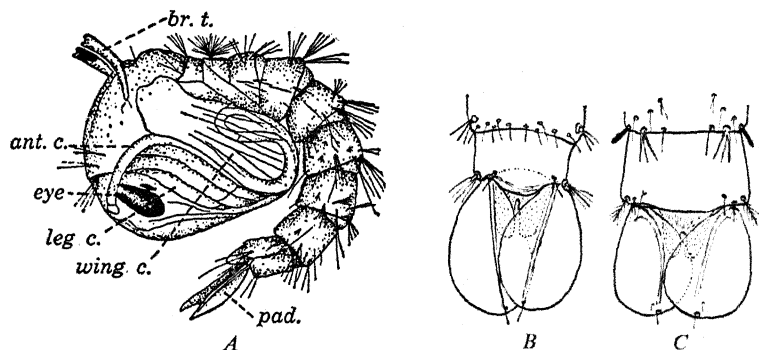


FIG. 232. A, pupa of *Culex pipiens*; ant.c., antennal case; br.t., breathing tubes; leg c., leg cases; pad., paddles; wing c., wing case. $\times 10$. (After Howard, Dyer, and Knab, *Carnegie Inst. Wash. Publ.*, 159, 1912-1917.) B and C, end of abdomen of pupae of *Aedes vexans* and of *Anopheles m. occidentalis*, respectively. *Anopheles* has peg-like spines at apical angles of all but last segment, and culicines have single tuft of branched fine hairs anterior to angle. (Adapted from Matheson, *Handbook of Mosquitoes of North America*, Comstock, 1944.)

Adult mosquitoes vary to a remarkable degree in habitats, feeding habits, mode of hibernation, choice of breeding grounds, and other habits. Knowledge of the habits and habitats of particular species is of great economic importance, since it does away with useless expenditure in combating harmless or relatively harmless species and aids in the fight against particularly noxious ones. The measures that would be required to control the breeding of the yellow fever mosquito, *Aedes aegypti*, would have little or no effect on *Anopheles quadrimaculatus*, and vice versa. Cutting down jungle to admit sunlight to water would eliminate malaria in some places but would be the best way to increase it in others. In dealing with mosquito-borne diseases or mosquito plagues it is obvious, therefore, that the particular species involved should be determined and their habits thoroughly understood.

Ecological Groups. Because of their variable breeding habits and choice of breeding places, their different tastes in blood, and the different extent of their travels, the various species of mosquitoes have very

different relations to human beings. The majority that are annoying to man can conveniently be divided into a number of general groups. Only a few species can be considered *house mosquitoes*, i.e., species that live and breed primarily in and around houses, and therefore tend to be urban and domestic. *Culex pipiens*, the closely related *C. fatigans* (= *C. quinquefasciatus*), and *Aedes aegypti* are common widely distributed household mosquitoes. These species tend to be very local, seldom scattering more than a few hundred yards, so that people at 2100 Main Street may complain bitterly of mosquitoes, while those at 2500 Main Street may rarely see one. They can usually be controlled by searching for and eliminating or treating breeding places on one's own or adjoining premises. In the Orient *Aedes albopictus* and *A. scutellaris*, which belong to the same subgenus as *A. aegypti* (*Stegomyia*), are also house mosquitoes. Some *Anopheles* also fall in this category, mostly in rural areas, e.g., *A. quadrimaculatus* and *A. maculipennis freeborni* in the United States, *A. darlingi* in South America, *A. gambiae* in parts of Africa, and *A. stephensi* in India; the last is a true urban species.

Marsh and swamp mosquitoes are likely to be more annoying outdoors, but some species freely invade houses, either for food or for shelter. The salt marsh mosquitoes lay their eggs in dry depressions; hatching occurs after rains, floods, or high tides. The advent of a heavy rain after a dry spell may cause the egg production of weeks to hatch, and billions of mosquitoes are produced simultaneously. Marshes on the east coast of Florida may average 30 to 50 million larvae per acre. Under favorable conditions of temperature, humidity, and breeze they migrate inland for as much as 30 or 40 miles and literally blanket the country for miles. Towns in their path have a veritable plague of mosquitoes, but it seldom lasts more than a few days. Only large-scale, pre-invasion attacks have any effect on the salt-marsh mosquitoes. The principal members of this group are two species of *Aedes* (*sollicitans* and *taeniorhynchus*) distinguishable from other common species in the United States, except for some of the large, metallic-colored *Psorophora*, by a white band on the proboscis and striped legs. *A. sollicitans* has a median dorsal white stripe on the abdomen, *taeniorhynchus*, which also breeds in fresh water, only black and white cross-bands. *A. dorsalis* is a small brown mosquito without a band on the proboscis but with the tarsal segments banded at both ends; it is a salt-marsh species on the northwest coast but breeds in fresh water in the northern interior.

The species of *Psorophora*, along with *A. taeniorhynchus*, breed in temporary rain pools in meadows and may become extremely abundant

4 or 5 days after a heavy rain. Some species of *Psorophora*, including the huge "gallinipper," are predaceous on other mosquito larvae. Annoying species which breed in swamps, seepage or overflows from drainage ditches, flood waters, rice fields, etc., are *Culex territans* and *salinarius* in the East and *C. tarsalis* in the West, the widely distributed *Aedes vexans*, species of *Theobaldia* and *Mansonia*, and most species of *Anopheles*. These, and many other species of northern *Aedes*, many of which have but one brood a year (but what a brood!), are the scourge of all rural residents, as well as picnickers, campers, hunters, and fishermen.

There are also a number of forest species which either breed in tree holes or in tree-top bromeliads (plants growing on the bark of trees). To this group belong the malaria-carrying *Anopheles bellator* and *cruzi* of Trinidad and Brazil, the brilliantly colored species of *Haemagogus* that are vectors of jungle yellow fever in South and Central America, and also various *Aedes* that carry this disease, especially *A. leucocelaeus* in South America and *A. simpsoni* and *A. africanus* in Africa.

Breeding Places. The breeding places of mosquitoes include practically any kind of water except the open sea; some species show very little preference, whereas others seem to be unreasonably choosy. There are species which breed in reedy swamps, woodland pools, eddies of rivers, slow-flowing streams, holes in trees, pools of melted snow, salt marshes, tide pools, crab holes, pitcher plants, treetop bromeliads, broken bamboo stems, coconut shells, or artificial containers from tin cans to cisterns and flooded basements. The species of *Mansonia* breed only in pools in which certain water plants grow, especially water lettuce (*Pistia*) or water hyacinths.

Some species breed only in pure clear water, others prefer filthy water; some breed only in sunlit water, others only in the shade; some demand quiet water, others breed only in flowing streams. Sometimes, of apparently similar pools, some will produce vast numbers of mosquitoes whereas others are left uninhabited; for the most part nobody knows why. Attempts have been made to correlate the preferences shown by mosquitoes with food, acidity or alkalinity, oxygen concentration, dissolved solids, etc., but with little success. The complexity of the problem is great, for odors may attract or repel the females searching for places to lay eggs; substances in the water may be directly injurious to the larvae; or, what is probably usually the dominant factor, the quantity or quality of the food may or may not be suitable. Most mosquito larvae, however, are able to use a considerable variety of foods, though living organisms are usually preferred. Barber successfully reared certain larvae on algae, bacteria, or ciliates alone.

Biological control of mosquitoes may eventually be possible, but so far only the surface has been scratched.

Migration. As already noted, the distance mosquitoes travel from their breeding places varies greatly with the species; knowledge of this is of great importance in connection with control. *Aedes aegypti* is seldom abundant more than a city block away from its breeding place, and the house-frequenting species of *Culex* seldom more than a few hundred yards. The writer has repeatedly been impressed with the fact that when mosquitoes are continuously complained of in cities, a breeding place can almost invariably be found within a block and often in the immediate vicinity. Most *Anopheles* make nightly migrations but seldom appear in appreciable numbers more than half a mile to a mile from their breeding places; a few species are known to migrate up to 10 miles. The yellow fever-carrying *Haemagogus* of South America travel at least 4 to 6 miles. *Aedes* on northern prairies are attracted by moving herds of animals and may follow them for many miles. Salt-marsh mosquitoes, however, are the only really migratory species, sometimes going 30 to 40 miles from home (see p. 702). *A. aegypti* is annually carried inland from the Gulf Coast by trains and busses and to northern ports on ships. Hawaii originally had no mosquitoes, but three species, *Culex fatigans*, *Aedes aegypti*, and *A. albopictus*, have been introduced with sailing vessels. In 1930 the deadly African malaria transmitter, *Anopheles gambiae*, was introduced and established in Brazil, as it was some years earlier in Mauritius and the Seychelles and later in Egypt.

Time of Activity. Although mosquitoes are usually thought to be nocturnal, and though this is true of most of the common species of temperate climates, it is by no means characteristic of the whole group. Many species, including most *Anopheles* and *Aedes scutellaris*, are active chiefly at twilight in the evening or early morning. Knab found that the mosquitoes of northern prairies, where the nights are too cold for them, are active throughout the day only. A large proportion of forest-living tropical species, at least in America, are diurnal. Some of the mosquitoes of the northern woods are apparently always ready to bite when a victim approaches, whether it be day or night. *Aedes aegypti* feeds by preference in the early morning or late afternoon. Here again a knowledge of the habits of particular species is important, since it may aid in the intelligent avoidance of disease-carrying forms.

Food Habits. Heretical as it may sound, mosquitoes feed mainly on plant juices, honey, etc. Philip found flowers, e.g., goldenrod, to be good collecting places for all but *Anopheles* mosquitoes. All adult males are strictly vegetarians and some females are also, e.g., *Toxorhyn-*

chites (= *Megarhinus*), which, however, is strictly cannibalistic on other mosquito larvae in its larval stage. Most females, although also feeding on nectar, etc., are bloodsuckers, and some require blood before they can lay fertile eggs. Dining on blood is not, however, always a necessary prelude to maternity; a domestic "citified" variety of *Culex pipiens*, *C. molestus*, is autogenic, i.e., oviposits without the need of blood meals. Roubaud bred twenty generations of this species without ever allowing the adults to feed at all. Some species indiscriminately attack any warm-blooded or even cold-blooded animal, but others show strong preferences. *Aedes spencerii* of our northern prairies flies towards any large object which its instinct leads it to suspect as a source of food. The importance of various species of *Anopheles* as malaria transmitters (see pp. 202, 712) depends largely on the extent to which they choose man as food. This is why *A. gambiae* is more dangerous than *quadrimaculatus*, and *quadrimaculatus* than *punctipennis*. *Anopheles gambiae* is one of the few species showing a strong preference for human blood. *Aedes aegypti* shows no distaste for man but readily bites other mammals, birds, and even cold-blooded animals.

Hibernation. The method employed by mosquitoes for passing the cold or dry seasons varies with the species. Many mosquitoes of temperate or tropical climates hibernate or pass the dry season as adults, the females stowing themselves away in hollows in trees, caves, crevices in rocks, cellars, barns, etc., to come forth and lay their eggs in the spring. A few species hibernate in the larval stage; *Wyeomyia smithii* larvae become enclosed in solid ice in the leaves of the pitcher plant in which they live. Most hibernating larvae retire to the bottom of their breeding pools during cold weather and do not survive freezing. Many temperate- and warm-climate mosquitoes and all northern ones pass the unfavorable season in the egg state, which may be looked upon as the *common* method of hibernation. Most *Anopheles* survive the cold season either as adults or as larvae but usually not as eggs.

Length of Life. The length of life of mosquitoes varies with the species and the sex. Male mosquitoes seldom live more than 1 to 3 weeks; their duty in life is done when they have fertilized the females. Paradoxically, the more favorable the conditions the shorter the lives of the females. They die soon after all their eggs are laid; with plenty of blood meals and readily available breeding places this may be only 3 or 4 weeks, whereas under less favorable conditions it may be several months. The species which lay all their eggs in a mass at one time are short-lived and have several generations a year, whereas those in which the eggs are laid in small lots at intervals live for several

months. Species in which the females hibernate are still longer-lived, but since they are not active in winter their *effective* life may be short.

Classification

More than 2000 species of Culicidae have been described, the majority of which belong in the tropics, although the north is richer in individuals; over 120 species have been described in the United States and Canada. There are two subfamilies, the Corethrinae, with a short non-piercing proboscis, and the Culicinae, including all the true mosquitoes. The further divisions into tribes and genera are shown in the following key, which is provided for the identification of the genera found in North America and of the more common or important species:

Key to Adults of North American Genera of Mosquitoes, with Notes on Commonest Species

- I. Tribe **Sabethini**. Postnotum (Fig. 233, *postn.*) with tuft of setae; tropical, non-bloodsucking species, breeding in water-holding plants; two widespread species in North America . . . *Wyeomyia smithii* and *W. haynei*. (Palpi short in both sexes; very small; color metallic, with underside of abdomen, tips of middle legs, and spot on top of head silvery white; breeds in pitcher plants.)
- II. Tribe **Anophelini**. Postnotum without setae; scutellum not lobed (Fig. 233D); palpi long in both sexes (Fig. 226); wings usually spotted or mottled; resting position usually not humpbacked; proboscis nearly parallel with axis of body (Fig. 237, *bottom*); only 1 genus . . . *Anopheles*. (Key to 11 North American species or varieties on p. 716.)
- III. Tribe **Culicini**. Postnotum without setae; scutellum trilobed (Fig. 233C); palpi short in female; wings rarely spotted, never mottled; resting position humpbacked (Fig. 237, *bottom*).
 - 1a. Proboscis rigid, down-curved (Fig. 233E) . . . *Toxorhynchites*. (Large, brilliantly colored, non-bloodsucking species, mostly tropical; 1 species in east and south, breeding in tree holes.)
 - 1b. Proboscis flexible, not curved . . . 2.
 - 2a. Second marginal cell ("2nd m." in Fig. 233B) less than half as long as petiole; palpi short in both sexes . . . *Uranotaenia*. (Small, tropical, non-biting, pool-breeding mosquitoes.)
 - 2b. Second marginal cell over half as long as petiole (Fig. 152D) . . . 3.
 - 3a. Spiracular bristles present (Fig. 233A); size large; metallic colors present or absent . . . 4.
 - 3b. Spiracular bristles absent; size medium or small; no metallic colors . . . 5.
 - 4a. No postspiracular bristles (Fig. 233A); size large; color not metallic . . . *Theobaldia*. (1 common species on west coast, *T. incidens*, which has dark spots on wings, banded abdomen, and unstriped legs.)
 - 4b. Postspiracular bristles present; size usually large; metallic colors present . . . *Psorophora*. (One species, *P. ciliata*, is largest mosquito in United States.)

- 5a. Fourth joint of front tarsi very short *Orthopodomyia*.
 (Tree-hole breeders, mostly in tropics. The one species in the United States has thorax with 6 narrow white lines and striped legs.)
- 5b. Fourth joint of front tarsi normal 6.
- 6a. Female with tip of abdomen truncated or blunt (Fig. 233G) 7.

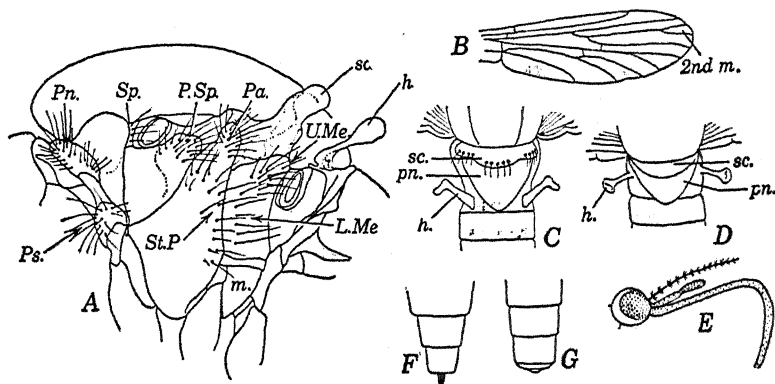


FIG. 233. Details of adult mosquitoes to illustrate key. A, thorax of *Psorophora* showing plates and groups of bristles used in distinguishing genera; h., haltere; l.me. and u.me., lower and upper mesepimeral bristles; pa., prealar; pn., pronotal; ps., prosternal; p.sp., postspiracular; sc., scutellum; st.p., sternopleural. B, wing of *Uranotaenia* with short 2nd marginal cell (2nd m.); C, trilobed scutellum (sc.) of culicines. D, scutellum of anophelines, without lateral lobes. E, head of *Toxorhynchites* (= *Megarhinus*) with curved proboscis. F, end of abdomen of *Aedes* ♀. G, end of abdomen of *Culex* ♀. (A, adapted from Matheson, *Handbook of the Mosquitoes of North America*, Comstock, 1944.)

- 6b. Abdomen of female pointed, with exerted cerci (Fig. 233F); eggs laid singly out of water *Aedes*.
 (Three main ecological groups: (1) tree-hole breeders (*Stegomyia*), from which *A. aegypti* was derived; (2) salt- or fresh-water marsh species with successive broods; (3) single-brood species breeding in spring pools from eggs laid previous summer.)

Common North American species:

- (a) *aegypti*; black with white striped legs and abdomen; black proboscis; lyre-shaped mark on back of thorax.
- (b) Salt-marsh mosquitoes; *sollicitans* and *taeniorhynchus* with white band on proboscis, *sollicitans* brown with median stripe on abdomen, *taeniorhynchus* darker, abdomen barred black and white; *cantator* with less prominent leg bands and no stripe on proboscis, confined to Atlantic coast.
- (c) *vexans*; fresh-water marsh and floodwater breeder, favoring filthy water; thorax bronze, abdomen black with white stripes; tarsi with very narrow white rings; widespread in United States and Canada.
- (d) *dorsalis*; in salt marshes and on western plains; tarsi white-ringed on both ends of joints; abdomen white-scaled, with two black patches on each segment; northern United States and Canada.

(e) *spring pool-breeders*: numerous species, without the combination of characters of above species.

- 7a. Female abdomen truncated; palpi of female usually one-fourth as long as proboscis or longer; wing scales large and broad *Mansonia*.
(Vicious biters in New World tropics, especially *M. titillans*, which reaches southern Texas and Florida; 1 species, *M. perturbans*, widely distributed in North America, has white-striped abdomen and legs, yellow band on proboscis.)
- 7b. Female abdomen blunt (Fig. 233G); palpi less than one-fifth as long as proboscis; wing scales narrow *Culex*.
(a) Brown species with proboscis and legs unstriped; abdomen with distinct white bands; common in and about houses; *pipiens* and *territans* in north, *fatigans* in south.
(b) Similar, with very narrow or no bands on abdomen; breeds in marshes; less domestic; *salinarius* in eastern United States.
(c) Proboscis with white band; abdomen and legs white-striped; breeds in ground pools, seldom enters houses; *tarsalis* in western United States.

Identification of Larvae of Common or Important North American Species

Anopheles Larvae. No breathing siphon (Fig. 231); lie parallel with surface. (See Fig. 234 for other anatomical details mentioned in key.)

- 1a. Both pairs of anterior clypeal bristles simple or slightly feathered 2.
1b. Outer pair of anterior clypeal bristles profusely branched; leaflets of palmate hairs notched at tip 3.
- 2a. Both pairs of anterior clypeal bristles slightly feathered; leaflets of palmate hairs narrow, pointed; palmate hairs on all of first 7 abdominal segments, those on first small *albimanus*.
2b. Both pairs of anterior clypeal bristles simple; leaflets of palmate hairs narrowed to slender point at tip; palmate hairs rudimentary on first and second segments, all about same size on other segments *pseudopunctipennis*.
- 3a. Inner clypeal hairs close together at base 4.
3b. Inner clypeal hairs separated at base 9.
- 4a. Inner clypeal hairs forked beyond middle; in northern United States and Canada, west to continental divide *maculipennis earlei*.
4b. Inner clypeal hairs single 5.
- 5a. Palmate hairs well developed on only 3 segments (4-6); southeastern United States *crucians georgianus*.
5b. Palmate hairs well developed on 5 segments (3-7) 6.
- 6a. Pecten with no more than 2 or 3 small teeth between long ones 7.
6b. Pecten with 3 to 5 small teeth between long ones 8.
- 7a. Hairs 0, 2, 3, and 4 on 4th abdominal segment all well-developed, branched *crucians crucians*.
7b. Hair 0 very small, hair 2 usually single *crucians bradleyi*.
- 8a. Posterior clypeal hairs double; antepalmate hair (2) double or triple *punctipennis*, *maculipennis freeborni*.
8b. Posterior clypeal hairs multiple, antepalmate (2) of fourth abdominal segment usually single; on west coast *occidentalis*.

- 9a. Antepalmate hair (2) of 4th abdominal segment usually single; south-eastern United States *quadrimaculatus*.
 9b. Antepalmate hair (2) of 4th abdominal segment multiple; central valley of Mexico *maculipennis aztecus*.

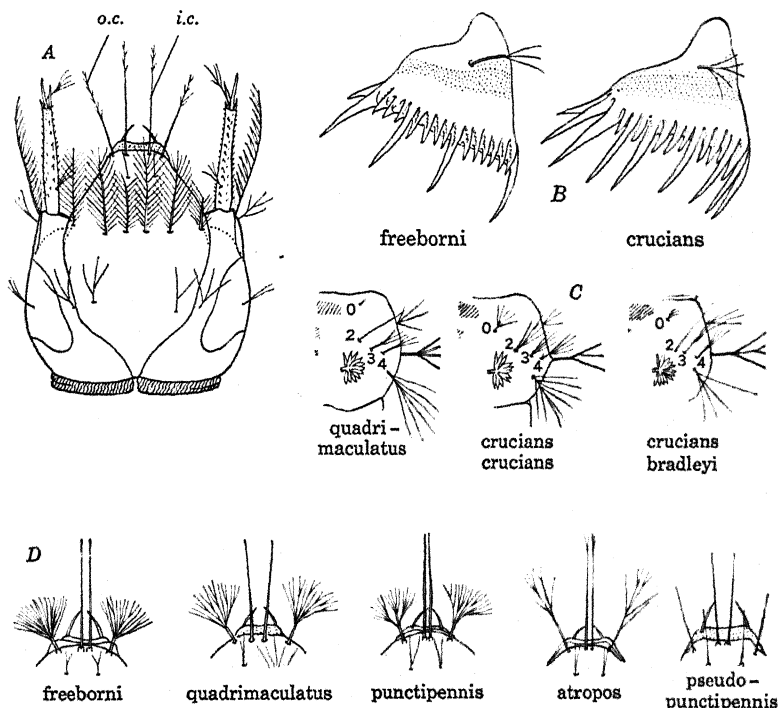


FIG. 234. Details of North American *Anopheles* larvae to illustrate key. A, head, showing hairs; i.c., inner clypeal hairs; o.c., outer clypeal hairs. B, pectens. C, fourth abdominal segments showing hairs 0, 2, 3, and 4 (hair 1 is the palmate hair). D, clypeal region of various species. (Adapted from Ross and Roberts, *Mosquito Atlas I*.)

Culicine Larvae. Breathing siphon present (Fig. 231A). See Fig. 235 for other anatomical details mentioned in key.

- 1a. Breathing siphon spine-like at tip, used to pierce air channels in roots of aquatic plants; larvae do not come to surface *Mansonia*.
 1b. Breathing siphon normal 2.
 2a. Anal segment with no ventral brush *Wyeomyia*.
 2b. Anal segment with ventral brush 3.
 3a. Siphon without pecten; anal segment ringed by chitinous band; chitinous plate on eighth segment also 4.
 3b. Siphon with pecten 5.
 4a. Mouth brushes modified into coarse prehensile lamellae, hooked for seizing prey; plate on eighth segment with 2 spiny hairs; in tree holes *Toxorhynchites*.

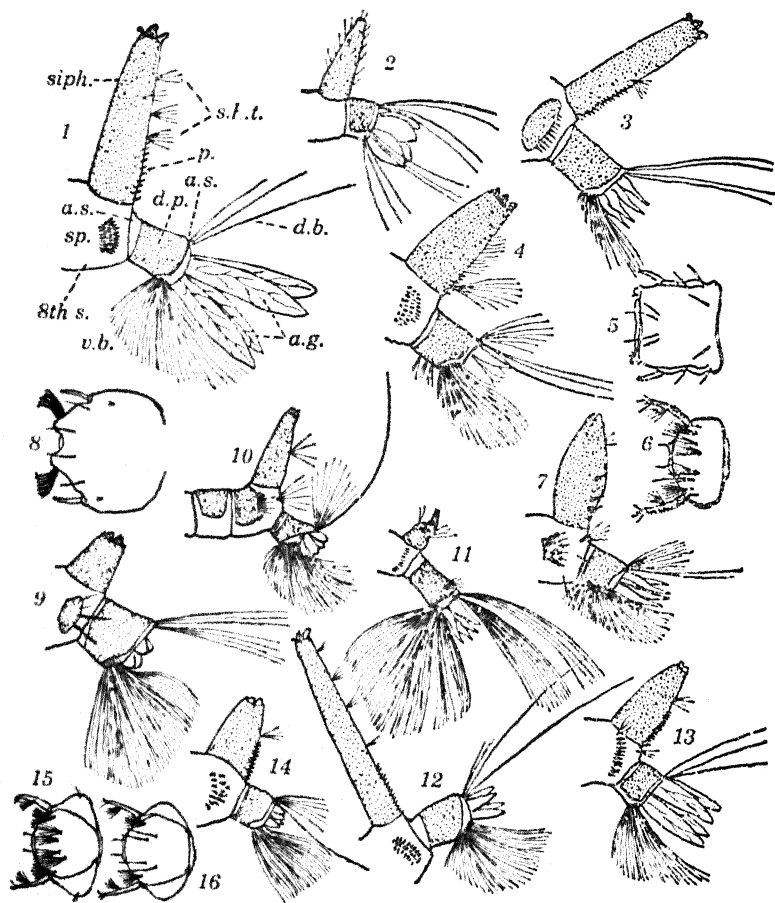


FIG. 235. Details of structure of culicine larvae to illustrate key. (Adapted from Dyar, *Carnegie Inst. Wash. Publ.* 387.) 1, posterior portion of larva of *Culex fatigans*; a.s., anal segment; 8th s., eighth segment; a.g., anal gills; d.b., dorsal brush; d.p., dorsal plate (a complete ring in this and many other species); p., pecten or comb; siph., siphon; sp., patch of spines on eighth segment; s.f.t., siphonal hair tufts. 2, *Wyeomyia smithii*, posterior end. 3, *Uranotaenia sapphirinus*, posterior end. 4, *Theobaldia incidens*, posterior end. 5, *Psorophora ciliata*, head. 6, *Psorophora (Janthinosoma) columbiae*, head. 7, *Psorophora (Janthinosoma) columbiae*, posterior end. 8, *Toxorhynchites (=Megarhinus) septentrionalis*, head. 9, *Toxorhynchites (=Megarhinus) septentrionalis*, posterior end. 10, *Orthopodomyia signifera*, posterior end. 11, *Mansonia perturbans*, posterior end. 12, *Culex salinarius*, posterior end. 13, *Aedes aegypti*, posterior end. 14, *Aedes taeniorhynchus*, posterior end. 15, *Aedes canadensis*, head. 16, *Aedes dorsalis*, head.

- 4b. Mouth brushes normal; double row of stout spines on eighth segment; in water-holding plants or tree holes *Orthopodomyia*.
- 5a. Siphon with several pairs of ventral tufts; anal segment ringed; siphon usually at least 4 or 5 times as long as wide *Culex*.
- a' Antenna with tuft at or before middle; all but one of ventral tufts of siphon represented by single hairs *territans*.
- a'' Antenna with tuft well beyond middle; several tufts on siphon b.
- b' Siphon 7×1 *salinarius*.
- b'' Siphon 5×1 or less c.
- c' Siphon with 5 hair tufts, all in line *tarsalis*.
- c'' Siphon with 4 hair tufts, third out of line *pipiens* and *fatigans*.
- 5b. Siphon with a single pair of ventral tufts 6.
- 6a. Anal segment ringed; spines of eighth segment attached to posterior margin of a chitinous plate *Uranotaenia*.
- 6b. Spines of eighth segment not attached to a chitinous plate 7.
- 7a. Spines of distal part of pecten produced into long hairs; hair tuft at base of siphon *Theobaldia*.
- 7b. Pecten of short spines; hair tuft near middle of siphon or beyond 8.
- 8a. Anal segment ringed by chitinous plate, and ventral brush partly inserted into it; in temporary rain pools *Psorophora*.
- (a) Mouth brushes prehensile; antennae not projecting anterior to head; predaceous; very large subgenus *Psorophora*.
In North America two spp., *ciliata* and *howardi*.
- (b) Mouth brushes normal, and antennae large; size smaller; several common United States species subgenus *Janthinosoma*.
- 8b. Anal segment not ringed, or if ringed, ventral brush posterior to it *Aedes*.
- a' Pecten with teeth detached outwardly; antenna spined all over; siphon 3×1 *vexans*.
siphon $2\frac{1}{2} \times 1$, on northern prairies *spencerii*.
- a'' Pecten without detached teeth b.
- b' Comb scales 8 to 12, in a single row; anal segment not quite ringed; head hairs all single; anal segment short *aegypti*.
- b'' Comb scales in triangular patch c.
- c' Anal segment ringed d.
- c'' Anal segment not ringed e.
- d' Siphon about 2×1 *solicitans*.
- d'' Siphon less than 2×1 *taeniorhynchus*.
- e' Anal segment nearly twice as long as wide; head hairs single or double; anal gills large, *stimulans*; anal gills very small *dorsalis*.
- e'' Anal segment about $1\frac{1}{2}$ times as long as wide; head hairs multiple *canadensis*.

Mosquitoes and Malaria

Anopheles mosquitoes are the sole transmitters of human malaria, which at least until recently has ranked as the most important human disease in the world. Species of *Culex* and *Aedes*, and less frequently *Anopheles*, are vectors of malaria of birds and reptiles (see p. 184). The role of mosquitoes in transmitting human malaria has been sus-

pected by various peoples as far back as any records go. The steps which led to the *proof* of it are briefly outlined on pp. 185-186.

The genus *Anopheles* contains numerous species, and they are divided into a number of subgenera. The majority of the species can be experimentally infected with malaria parasites, but some much more readily than others. There is also a difference in the facility with which certain species can be infected with different malarial species and strains (see p. 203). Mere experimental infection of an insect with a disease germ or even successful transmission by it under experimental conditions means very little with respect to its role in nature. Many other factors come into play which cannot be studied in the laboratory and the combined effect of which can be learned only by extensive and carefully studied epidemiological evidence. *A. punctipennis*, for example, though a proved transmitter of malaria in the laboratory, is eliminated in nature by its habits. It is a "wild" species which seldom enters occupied houses and which shows a strong preference for animal over human blood.

In Europe the common and widespread *A. maculipennis* is not a uniform species but consists of a number of biologically distinct races, now sometimes considered species, some of which are dangerous malaria vectors whereas others are in most places practically harmless. These races of *maculipennis* differ in coloration of eggs and other minor morphological characters and in such biological ones as breeding in fresh or brackish water, hibernation, and—most important—in willingness to feed on man instead of cattle.

In Europe *A. m. labranchiae*, which breeds in both fresh and brackish water, and has wedge-shaped black spots on the eggs, is a man-eater and was the most important malaria transmitter in southern parts. *A. m. atroparvus*, which breeds by preference in brackish water, was an important vector in the north and west coasts of Europe. The other European varieties are mainly zoophilic, but may bite man sufficiently to keep malaria going in backward areas where domestic animals are scarce. With the extensive control or even eradication of the more domestic species, as in Italy and Sardinia, the more zoophilic outdoors species may become relatively more important.

In North America, *A. quadrimaculatus* of the southeastern states, and the only important potential malaria vector in that area, is closely related to *maculipennis*, but is regarded as a distinct species. There are four other mosquitoes which are considered only subspecies of *maculipennis*. These are *earlei* in northern United States and Canada west to the Rockies; *freeborni* in the west between the Coast Range and the Rockies, except in the south where it extends from the southern

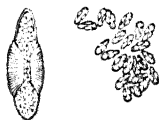
California coast to southwest Texas; *occidentalis* on the Pacific coast from central California to Alaska; and *aztecus* in the central valley of Mexico. Of these only *freeborni* and *aztecus* are (or were) malaria vectors; these two have wings all dark whereas the others have a lighter coppery spot at the tip of the wing.

A. maculipennis is not alone in being composed of races differing in their feeding and breeding habits. Several of the "big shots" in the transmission of malaria, including *A. sinensis*, *maculatus*, *aquasalis*, *pseudopunctipennis*, and perhaps *gambiae* and *funestus*, behave differently in one place than in another. In the United States *pseudopunctipennis* is an apparently harmless species, but in mountainous regions from Mexico to Argentina it is Public Enemy No. 1 among the anophelines.

Information on food preferences of *Anopheles* can be obtained by precipitin tests of the blood obtained from their stomachs. In tests on three common *Anopheles* in southeastern United States, of *A. quadrimaculatus*, the only malaria carrier, about one-third had fed on man, the majority on cattle; of *A. crucians*, only a little over 1 per cent had fed on man, the majority on cattle, pigs, horses, and dogs; and of the *A. punctipennis* examined, all had fed on animals. Of *A. pseudopunctipennis* examined in northern Argentina, where this species is an important vector, 50 per cent had fed on man, 21.8 per cent on dogs, and only 23 per cent on all the large domestic animals combined. The United States strain of this species would undoubtedly give very different results.

Identification of *Anopheles*. The *Anopheles* mosquitoes fortunately are fairly easy to identify in all stages of their development. The different species vary a great deal in choice of breeding places, habits, and appearance, so that it is necessary in any malarial district to determine which species are malaria carriers, how they may be identified, where they breed, and what their habits are. The majority of the species have mottled or spotted wings, and the arrangement of the markings is usually a good means of identification (Fig. 237).

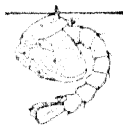
Figure 236 is a comparative table which shows in a graphic way how *Anopheles* may ordinarily be distinguished from other common mosquitoes, such as *Culex* and *Aedes*, in their different stages. The "floats" on the eggs of *Anopheles* are rarely absent; their size and markings sometimes serve as means of identification of species. Owing to the effects of surface tension the eggs of *Anopheles* tend to assume geometrical patterns on the surface of the water. The larvae, besides the absence of a breathing tube and their horizontal floating position at the surface of the water, have other identifying features such as

Anopheles

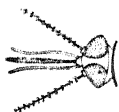
Eggs laid singly on surface of water; provided with a partial envelope, more or less inflated, acting as a "float."



Larvae have no long breathing tube or siphon; rest just under surface of water and lie parallel with it.



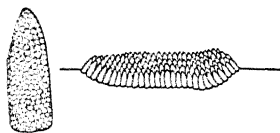
Pupae have short breathing trumpets; usually do not hang straight down from surface of water.



Palpi of both male and female long and jointed, equaling or exceeding the proboscis in both sexes.

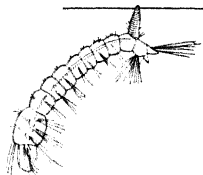


Adult rests with body more or less at angle with surface, the proboscis held in straight line with body.

Culex, Aedes, etc.

EGGS

Eggs laid in rafts or egg boats or singly on or near water or where water may accumulate; never provided with a "float."



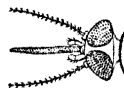
LARVAE

Larvae have distinct breathing tube or siphon on eighth segment of abdomen; hang from surface film by this siphon, except in *Mansonia*, which obtains air from aquatic plants.



PUPAE

Pupae have breathing trumpets of various lengths; often hang nearly straight down from surface of water.



HEADS OF ADULTS

Palpi of female always much shorter than proboscis, those of male usually long but sometimes short.



RESTING POSITION OF ADULT

Adult usually rests with body parallel to surface, though sometimes at an angle. Proboscis not held in straight line with body, giving "hump-backed" appearance.

FIG. 236. Comparison of *Anopheles* and culicine mosquitoes.

the rosette-like palmate hairs on some of the segments, which serve to hold the larvae in the characteristic position by surface tension. The species of *Anopheles* larvae are sometimes very difficult to identify, and reliance must be placed on the form, number, and distribution of characteristic hairs. A key to the American species is given on p. 708.

The pupae have short and more flaring breathing tubes than those of *Aedes* or *Culex*, the paddles at the end of the abdomen have an accessory hair in addition to the terminal one, and all but the last abdominal

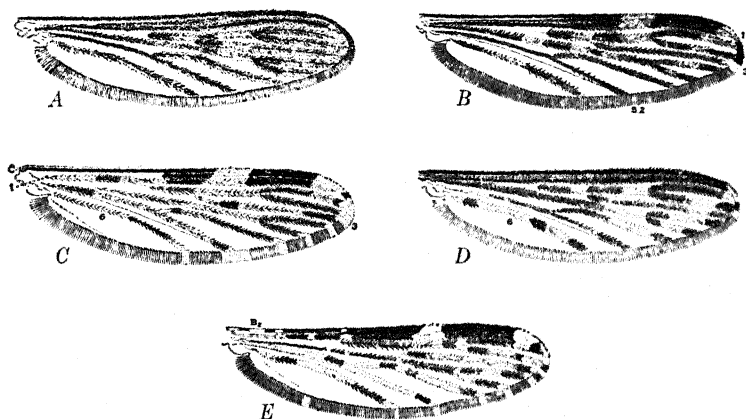


FIG. 237. Wings of North American *Anopheles*. A, *quadrimaculatus*; B, *punctipennis*; C, *crucians*; D, *pseudopunctipennis*; E, *albimanus*. (After Ross and Roberts, *Mosquito Atlas*, I.)

segment have peg-like spines on their posterior corners (Fig. 232). The pupae of some of the American *Anopheles* can be identified by coloration (Burgess, 1946). The adult *Anopheles* are usually easily distinguishable by the resting position, with the proboscis, thorax, and abdomen all in a straight line and at an angle to the resting surface, in contrast to the parallel or drooping abdomen and humpbacked appearance of culicines, but some of them, e.g., *A. culicifacies* of India, resemble the culicines in resting position. *A. quadrimaculatus* is more culicine-like than are other North American *Anopheles*; it rests at only a slight angle to the surface, whereas *punctipennis* appears almost to stand on its head. Most *Anopheles* have the wings marked with dark or light spots or both, but even this is not constant, since a few culicines have spotted wings and a few *Anopheles*, e.g., *A. atropos* and *A. walkeri*, have unspotted ones. The long palpus of the female is a character which can always be relied upon.

Following is a key for the identification of the North American

species north of Mexico, with comments on their distribution and importance:

- 1a. "White-footed" species with hind tarsi having last $3\frac{1}{2}$ segments all, or nearly all, white; wings marked with both black and white spots. Several species in tropical America, several being very important malaria vectors. Only species reaching Texas and southern Florida, and most important vector in West Indies and Central America *albimanus*.
- 1b. Dark-legged species without white stripes or areas on legs 2.
- 2a. Wings not spotted, or spots indistinct
 - (1) No white knee spots; inconspicuous rings on palpi; Gulf and Atlantic coasts, breeding in salt water; coloration very dark *atropos*.
 - (2) With narrow rings on palpi; eastern United States, breeding in fresh-water marshes; white knee spots; not important *walkeri*.
 - (3) Small; dark palpi; no white knee spots; breeds in tree holes *barberi*.
- 2b. Wings not uniformly colored 3.
- 3a. Wings with two or four dark spots; white knee spots 4.
- 3b. Wings with white or yellow spots along costal margin (Fig. 237C, D) 5.
- 4a. Apex of wing uniformly colored, dark; only important malaria carriers in United States in south, *quadrimaculatus*.
..... west of Rockies, *maculipennis freeborni*.
- 4b. Apex of wing with coppery spot in north states, *m. earlei*.
..... on Pacific slope, *m. occidentalis*.
- 5a. Only one white spot on costal margin, at tip of wing (Fig. 237A); anal vein with 3 black spots *crucians*.
- 5b. A large yellow spot on outer third of costal margin involving three veins, another at tip, and another in basal third; fringe nearly all dark; extends farther north than most species (Fig. 237C) *punctipennis*.
- 5c. Four yellowish white spots along front of wing; fringe of wing alternating black and white; southwestern United States to Argentina; not important in the United States, but principal transmitter in mountains from Mexico to Argentina *pseudopunctipennis*.

Habits of *Anopheles*. Most *Anopheles* breed in natural waters such as ponds, swamps, edges of streams, rice fields, and grassy ditches. Our species all breed in standing water, but this is not true everywhere. In Europe and Asia some of the most important species breed in flowing streams, which necessitates entirely different methods for their control. Some species breed in brackish water, some in shaded water, some only in sunlight, and a few in artificial containers around houses. Members of the subgenus *Kerteszia* breed in bracts of leaves of bromeliads growing on forest trees. Some *Anopheles* show much more pronounced preferences than others. *A. quadrimaculatus*, formerly the principal malaria vector in the southeastern states, is one of the least particular species. According to Hinman in 1940, optimum conditions for its breeding are afforded by clean, open water with dense aquatic vegetation and abundant flotage. Natural shade restricts the vegetation, thereby decreasing the protection and food of the larvae.

Shade-loving species of jungles and forests are *A. darlingi* of tropical America, *A. funestus* of Africa, and *A. umbrosus* of southeast Asia, whereas *A. albimanus* and *aquasalis* of tropical America, *A. gambiae* of Africa, and *A. barbirostris* of Asia breed only in sunlit waters. In Malaya the cutting down of jungle in the flat lands and exposure of sluggish water to sunlight changes a dominance of *umbrosus* to *barbirostris*, with a reduction in malaria; but when ravines in the hills are

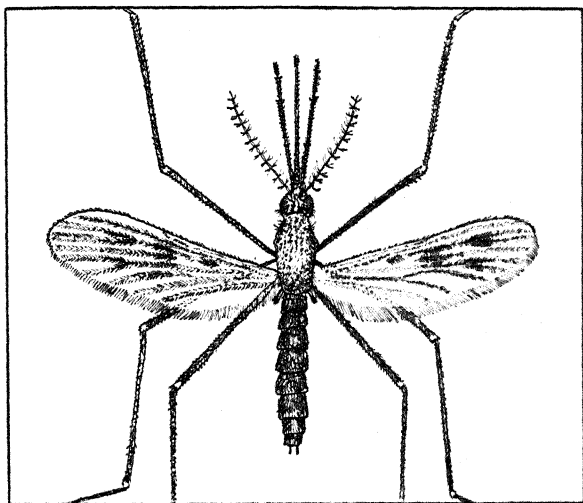


FIG. 238. *Anopheles quadrimaculatus*, in former days the principal malaria transmitter in southeastern United States.

opened up and the sparkling streams cleared of vegetation and exposed to sunlight, the harmless jungle species disappear and the deadly *A. maculatus* takes their place. Thus in the two localities directly opposite conditions determine the presence or absence of malaria. *A. sundaicus*, an important malaria carrier in southeastern Asia, breeds in strongly brackish or even concentrated sea water, as in the holes of mud lobsters or in sea water pools inside the reefs of coral islands. *A. bellator*, an important vector in Trinidad, breeds in aerial plants in trees planted to shade cocoa groves, and both this species and *A. cruzi* breed in bromeliads in forest trees in southern Brazil, and sometimes even in trees in towns.

The eggs of *Anopheles* are not as resistant to drying as those of *Aedes* but will survive for as long as 3 weeks on drying mud, and even the larvae can live on moist mud for some time. The eggs hatch only in water and at temperatures above 60°F.; under favorable conditions

they hatch in 1 to 2 days. The larvae are surface feeders; they seem to feed on any particles floating on or near the surface which are small enough to swallow. *Anopheles* larvae are not rapid in their development as compared with some mosquitoes; the time required under favorable conditions is 2 to 3 weeks or more. The number of generations a year probably varies greatly with the species and conditions of food and temperature. It has been estimated that *A. quadrimaculatus* has 8 to 10 annual generations in southeastern United States.

Adult *Anopheles* are for the most part twilight feeders; but there are many exceptions. Some species come forth with the first shade of late afternoon, others not until almost dark. A few species, e.g., *A. brasiliensis*, are diurnal; many forest species will bite willingly in the daytime if disturbed. The food preferences of adult females and their important bearing on malaria transmission have already been discussed. An important observation made by Roubaud is that the adults, at least of *A. maculipennis*, fly out into the open and invade other houses or sheds even if there is an abundant food supply where they have been resting after an earlier meal; as a result the *Anopheles* population of any spot is entirely changed in a few days; this flight in the open seems to be indispensable to the life of *A. maculipennis*, and it also has an important bearing on malaria transmission. Mosquitoes do not suck blood daily; usually blood meals are taken at intervals of several days.

Most *Anopheles* are rather sedentary in habit and seldom fly in numbers more than a fraction of a mile from their breeding places. *A. quadrimaculatus* is more of a traveler than most species, but even it rarely goes more than a mile from its breeding place, although occasionally in the fall before hibernation it may scatter in significant numbers up to 3 miles. *A. albimanus*, however, is reported to fly as far as 12 miles from Gatun Lake in Panama. Abundant *Anopheles*, nevertheless, usually indicate breeding places within a mile.

Anopheles hibernate either as adults in protected buildings, caves, or tree holes, or as larvae which bury themselves in mud or under debris at the bottom of water in ponds or marshes. The eggs do not live through cold winters.

Malaria-Carrying Species. About 200 species of *Anopheles* have been described, and a large percentage of them have been shown to be capable of transmitting malaria experimentally, but only about two dozen of them are important natural vectors of malaria, and some of these only in limited areas. Often the habits of the species, as already shown, are of more importance than the ability to transmit the disease under experimental conditions. The difference in ability of

some species of *Anopheles* to nurse one species or strain of malaria more readily than another still further complicates the task of evaluating the roles of different species, for a certain species of *Anopheles* may for this reason be an important transmitter in one place and not in another.

The methods used in determining the importance of particular species are various. The most valuable and reliable criterion is the relative number of individuals with infected salivary glands found in malarial houses. (For methods of dissecting mosquitoes for demonstration of oöcysts and sporozoites, see Barber and Rice, 1936.) Supplementary information is obtained by observations on breeding and feeding habits (aided by precipitin tests), relative abundance and coincidence with outbreaks of the disease, and experimental transmission in the laboratory.

In the United States, until malaria was eradicated as an endemic disease about 1952, *A. quadrimaculatus* in the southeast and *A. m. freeborni* in the arid west were the only important vectors. The principal vectors in other parts of the world are as follows: in Mexico, *pseudopunctipennis* on western slopes, *maculipennis aztecus* in the central valley, and *quadrimaculatus* and *albimanus* in humid coastal areas; in Central America and West Indies the white-footed *albimanus*; in Trinidad the bromeliad breeder, *bellator*; in South America, to south latitude 25 in the interior as well as on the coast, the highly domestic shade breeder, *darlingi*, and on the coasts *aquasalis*, breeding in sunlit brackish water, and *albitarsis domesticus*; in southern Brazil, the bromeliad breeders, *bellator* and *cruzi*; in the Andean region, *pseudopunctipennis*; in western Europe certain races of *maculipennis*, especially *labranchiae* and *atroparvus*, which breed in both brackish and fresh water; in the Balkans and Middle East, *superpictus*, breeding in flowing water in hills, *sacharovi* in brackish and fresh-water marshes, and *claviger* in marshes, cisterns, and wells; in Africa, *gambiae*, breeding in sunlight, and *funestus* in shade, and *pharoensis* in upper Egypt and Sudan; in India numerous species, particularly *culicifacies* (principal vector in Ceylon), *philippinensis*, *stephensi* (an urban species breeding in man-made containers), *varuna*, *sundaicus*, *minimus*, and *fluviatilis*; in southeast Asia the last three of these plus *aconitus*, *maculatus*, *latifer*, and *annularis*; in China, Japan, and Korea, *hyrcanus sinensis*, *minimus*, and *pattoni*; in Borneo, *leucosphyrus*; in the South Pacific and Australian region, *farauti* and *punctulatus* (but only in islands as far east as the New Hebrides; the oceanic ones farther east have no *Anopheles*). These species account for the majority of malaria in the world, but many other species also contribute and may be locally important.

The effect of anti-*Anopheles* campaigns on the prevalence of malaria is discussed in Chapter 9, pp. 207-209.

Mosquitoes and Yellow Fever

History and Nature of Yellow Fever. Once the scourge of the entire Western Hemisphere, yellow fever is now confined to forested areas of tropical America and to Central Africa. In Africa it was formerly thought to be limited to West Africa, but it also occurs in Sudan, and protection tests with serum show that it extends all the way to the Red Sea in Eritrea and south to northern Rhodesia. It is caused by a filtrable virus (see p. 233) which is present in the blood and available to mosquitoes only during the first 3 days of illness. After infection there is a short incubation period of 3 to 6 days, followed by severe headache and aches in the bones and a sudden fever with flushed and swollen face and dry skin. After 3 or 4 days the fever subsides and there is a period of calm, usually with development of severe jaundice and often a "black vomit" of blood and bile. The mortality in adults is high, but there are many inapparent cases in children in endemic areas, as shown by protective antibodies in the serum. A highly effective protective vaccine is available and has been used on a very large scale in rural South America and in West Africa and for troops in endemic areas.

The discovery of the transmission by *Aedes aegypti* in 1900 by the illustrious work of the American Yellow Fever Commission composed of Reed, Carroll, Lazear, and Agramonte ended what Soper (1937) called the "Dark Age" of yellow fever and began the "Golden Age," during which so much progress was made in the control of the disease that for a few months in 1927 it was thought to have been completely eradicated from the Western Hemisphere. Then came the "Age of Disillusionment," with the dramatic revelation that yellow fever exists in a jungle form, usually silent and unrecognized, over vast areas in tropical America, a situation later found to exist in Africa also. Forest animals, particularly monkeys (marmosets, saimiri, and howlers in America and many species in Africa) serve as natural reservoir hosts. Other animals are also susceptible, e.g., opossums, hedgehogs, and in Africa the bush baby, *Galago*. In America mosquitoes of the genus *Haemagogus* (see following section) that breed in the treetops serve as vectors. They seldom leave the forest canopy even to invade small villages, so human cases occur only among people actually working in or near the jungle, especially in felling trees, and in the absence of *Aedes aegypti* there is no spread from man to man.

A similar jungle form of the disease exists in parts of Africa, trans-

mitted to man on plantations by *Aedes simpsoni*, which breeds in axils of leaves, and among monkeys in forests by *A. africanus* and probably *A. vittatus*, which breed in rock pools. Other species of *Aedes* in both Africa and South America and a few species of *Eretmopodites*, *Mansonia*, *Culex*, and *Anopheles* are capable of acting as vectors, though only a few are efficient transmitters; among these are *Aedes luteocephalus* and *A. stokesi* in Africa, and *A. fluviatilis* and *A. leucocelaenus* in South America.

When persons with yellow fever enter a town or city where *Aedes aegypti* is prevalent, the disease changes from a sporadic to an epidemic form. This was the only kind of yellow fever known prior to about 1930. It was once the greatest scourge of the Western Hemisphere, not only in the tropical and semitropical areas where *Aedes aegypti* is at home, but also in such places as Boston and Philadelphia, where great epidemics broke out late in the year after *A. aegypti*, imported on sailing vessels in which they found abundant breeding places, had become numerous. The toll from yellow fever during the French attempt to build the Panama Canal was appalling.

Before the transmission by *A. aegypti* was discovered and means of control understood, epidemics raged in tropical cities until a high percentage of people were either dead or immune, and in temperate cities until frost stopped the mosquitoes. The last outbreak in the United States was in New Orleans in 1905, when for the first time an epidemic was stopped by intelligent human effort. No urban outbreak of yellow fever has occurred in the Americas since 1933, although small *aegypti*-transmitted outbreaks have followed jungle outbreaks several times. The jungle outbreaks tend to shift from place to place. After 40 years' absence, jungle yellow fever suddenly struck Panama like a bolt from the blue in 1948, and progressed wave-like in the Atlantic rain forests into Costa Rica, crossed to the Pacific side, and progressed back into Panama on that side, and northward into Nicaragua and Honduras, almost reaching the Guatemala border in 1955. It killed many monkeys and a few men as it moved. In 1954 jungle yellow fever struck Trinidad also.

It commonly requires 10 to 12 days for *Aedes aegypti* to become infective after becoming infected, although at high temperatures the period may be shortened to as little as 4 days. Transovarial transmission does not occur, but larvae exposed to liquid containing the virus develop into infective adults. In order to keep an epidemic going it is necessary to have a fairly high incidence of *A. aegypti*. Even where there are many non-immunes an epidemic subsides when the *aegypti* index, i.e., the number of premises on which it is breeding,

falls below 5 per cent. It is doubtful whether an epidemic would start if, by inspection and anti-*aegypti* work, the index were held to 2 or 3 per cent, as it can be without too great difficulty.

Since *A. aegypti* has a world-wide distribution in the tropics, there is grave danger of the introduction of yellow fever into places where it has not previously existed and where, because of the non-immune condition of the people, it would become a terrible scourge. With modern airplane traffic the introduction of yellow fever in infected mosquitoes into India, Malaya, or Australia from west Africa or Sudan or into North America from South America is an ever-present menace. In India reliance is placed on fumigation or spraying of boats and planes and strict quarantine of individuals coming from endemic areas; in our own country dependence is placed on fumigation, local *aegypti* control, surveillance of exposed persons, and availability of vaccine for whole populations if a case should appear. Control of *A. aegypti* in non-infected countries is important in order to lessen the danger of rapid spread if the disease *should* get in, but the South American countries, which have the jungle disease in their backyards, so to speak, cannot afford to stop short of extermination on a continental scale. Fróes (1947) has outlined plans for this ambitious project. Most of Brazil and all of Bolivia have already exterminated this dangerous mosquito. It has also been virtually exterminated in Khartoum, so there is little danger now of yellow fever being carried to Egypt by Nile steamers.

***Haemagogus* spp.** These vectors of jungle yellow fever in South America are closely related to *Aedes* but have brilliantly metallic colors. They lay eggs as do *Aedes*, and the larvae are very similar. In most of the species the males have short palpi like the females. A number of species have been found naturally infected with yellow fever and are good potential vectors. The most important vectors in Brazil are *H. spegazzinii*, which has a wide distribution, and a variety of it, *H. s. falco* (Fig. 239), which is common from northwestern Brazil to Central America. These two and *H. capricornii*, a more southern species which has been confused with the others, can only be distinguished by the male genitalia, so that to identify females it is necessary to have them lay eggs, rear them, and then microscopically examine the males. The thorax of all these species is metallic blue or greenish blue and the abdomen violet. These mosquitoes undoubtedly breed normally in tree holes or in vegetation in treetops, but the breeding places are very difficult to find. Komp (1952) observed that *H. s. falco* can adapt itself to breeding in such man-made places as water-filled hollows in fallen trees, hollow stumps, cut bamboo stems, etc.,

at ground level. In the dry season they are seldom seen until a tree is cut down, whereupon they frequently buzz about in considerable numbers. At the forest's edge and in clearings they tend to move down from the canopy and invade coffee plantations, etc., where men are working. *Haemagogus* species and also *Aedes leucocelaenus* have



FIG. 239. *Haemagogus spegazzinii falco*, chief vector of yellow fever in northern South America and Central America. (Drawn from a painting by Varela in Kumm, Osorno-Mesa and Boshell-Manrique, *Am. J. Hyg.*, 43, 1946.)

been recaptured 4 to 7 miles from points of release, so they could disseminate yellow fever in areas of small residual forests surrounded by open country. There is a suspicion that in Panama, in addition to the species of *Haemagogus*, certain species of *Sabethes* may also be involved.

Other than clearing forest over large areas there is no known method of control of these mosquitoes, and control of jungle yellow fever in man depends on wholesale vaccination of populations in endemic areas.

Biology of *Aedes aegypti*. This mosquito is a member of the subgenus *Stegomyia*, which contains a group of originally tree-hole-breeding mosquitoes, several of which (e.g., *albopictus*, *scutellaris*, *polynesiensis*, as well as *aegypti*) have become more or less domestic

and have adopted man-made containers as breeding places. *Aedes aegypti* was long known in medical literature as *Stegomyia fasciata*. It is a small black species, conspicuously marked with silvery-white on the legs and abdomen and with a white lyre-shaped design on the thorax (Fig. 240). The female has very short palpi which are white at the tip. The wings are clear and somewhat iridescent.

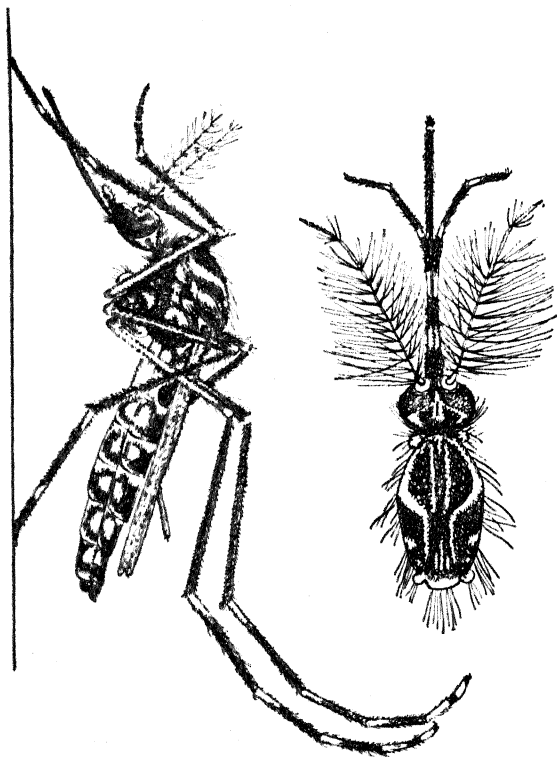


FIG. 240. *Aedes aegypti* ♀, and head of ♂. (After Soper and Wilson, *J. Natl. Malaria Soc.*, 1, 1942.)

Aedes aegypti is a "pet" mosquito, as domestic as a rat or a roach. It is almost never found more than a few hundred feet from human habitations, and feeds readily on human blood. Long familiarity with man has made it an elusive pest. Its stealthy attack from behind or under tables or desks; the suppression of its song; its habit of hiding behind pictures or under furniture; the wariness of its larvae—all these are lessons learned from long and close association with man. It is a diurnal mosquito, biting principally in the morning and late after-

noon, with a siesta in the middle of the day, but it will bite at night when hungry.

Life Cycle and Breeding Places. *Aedes aegypti* lays its eggs, after a blood meal, on the sides of a container, at or just above the water surface. A number of batches of eggs are laid, 10 to 100 at a time, usually at intervals of 4 or 5 days, until a total of 300 to 750 has been laid over a period averaging about 6 weeks. The average length of life of the adults is about 60 to 80 days.

Aedes aegypti has more completely forsaken its ancestral breeding places than any other mosquito, only rarely breeding in tree holes or broken bamboo stems but commonly utilizing rain-filled cocoanut shells around native villages, as well as artificial containers. It still prefers wood walls, such as those of barrels, but is also partial to earthenware or stone containers; clean glass or metal is less attractive but readily used when other containers are not available. Inside houses the most important breeding places are drinking-water jars, waterplants, neglected flower vases, unused toilets, and icebox drains; in residential yards they are cisterns, grease traps, tin cans, wide-mouthed jars, old tires, animal drinking pans, rain-water barrels, etc., and occasionally sagging roof gutters. In business or industrial areas they breed in barrels or buckets kept for fire protection, basement sumps, elevator pits, trash piles, etc., and in neglected spittoons. Neglected flower containers in cemeteries are a special menace. In places without a piped water supply, barrels or urns containing drinking water, tanks, and wells with wood, brick, or stone sides are important. Other places are the holy-water fonts in churches and the bilges of boats.

In the southern United States, *A. aegypti* survives the winter in the egg stage in dry containers, some even resisting freezing. Those in wet containers, as Hatchett in 1946 found in Houston, are in a precarious situation since they hatch during warm spells and are then killed later by cold spells. The larvae survive in fire barrels and other protected and more or less permanent receptacles or in large cisterns in which the water does not become too cold. These "mother foci" are also important in seeding secondary, less permanent, containers during the summer. Since this mosquito seldom flies more than a few hundred feet, although a few are often carried by cars, trains, or boats, its presence in numbers indicates a breeding place close at hand.

The eggs require several days for development of the embryo, and then they hatch within a few minutes after being submerged. Often when containers are filled with fresh drinking water, larvae appear almost at once. The eggs remain viable in the dry state for at least a year, but when wetted, all may not hatch; some may require several

wettings. Hatching does not occur readily in perfectly fresh water, but it is favored by presence of bacteria. The larvae (Fig. 241), however, do not thrive in very filthy water such as *Culex fatigans* delights in, but will tolerate considerable amounts of acid, alkali, or salt.

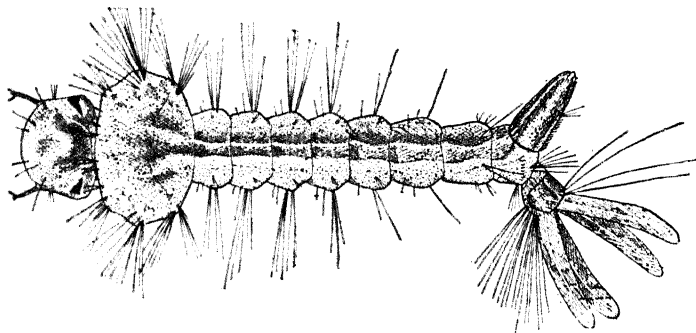


FIG. 241. Larva of *Aedes aegypti*, $\times 10$. (After Howard, Dyar, and Knab, *Carnegie Inst. Wash. Publ.*, 159, 1912-1917.)

When disturbed, even by a shadow, the larvae swim to the bottom, which they hug so closely that if a container is dumped, a large proportion of them may remain in a cupful of water that is left behind. Under favorable conditions the time from egg to egg is about 16 days—2 to 3 for hatching, 5 to 6 for the larvae, $1\frac{1}{2}$ to 2 for the pupae, and 6 to 7 before the adult lays eggs again.

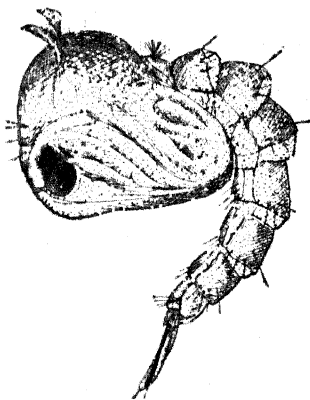


FIG. 242. Pupa of *Aedes aegypti*, $\times 10$. (After Howard, Dyar, and Knab, *Carnegie Inst. Wash. Publ.*, 159, 1912-1917.)

Aedes aegypti probably originated in Africa, but it has followed man to all parts of the world because of its tendency to "stow away" in boats, trains, airplanes, and automobiles. It is a permanent resident in all tropical and subtropical parts of the world and is annually carried to places far outside its permanent range. In the United States it lives through the winter in sufficient numbers to become abundant

early in the season only on the Gulf Coast, but it survives in numbers sufficient to produce a good population late in the year in many interior cities. In the Oriental region, for some unknown reason, it does not thrive so well as other domestic members of the *Stegomyia*

group—*scutellaris*, *pseudoscutellaris* and *polynesiensis* in the South Pacific islands, and *albopictus* in southeast Asia and Honolulu.

Control of *Aedes aegypti*. Since this mosquito breeds almost exclusively in artificial containers, special control measures apply to it. Drainage, filling in, airplane dusting, and large-scale oiling, so useful for malarial and other ground-breeding mosquitoes, have no part in *A. aegypti* control. The principal useful methods are: (1) turning "bottoms up," destroying, or removing miscellaneous containers exposed to rain; (2) emptying animal drinking pans, icebox drip pans, flower vases, water plants, spittoons, etc., frequently; (3) keeping drinking water in jars, barrels, etc., constantly covered with cloth except when dipping water; (4) sealing up, filling up, draining, or destroying unused cisterns and tanks where feasible; (5) mosquito-proofing used overhead cisterns and stocking attic or underground cisterns and wells with *Gambusia*; treating water in fire-protection buckets or barrels, stranded boats, etc., with larvicides; puncturing or straightening sagging roof gutters; and stocking concrete fish ponds or lily ponds with *Gambusia*.

For cisterns or other drinking containers where water can be drawn off from below and which for any reason cannot be mosquito-proofed, oil applied to the surface at weekly intervals is most satisfactory. Addition of 1 cc. of 2 per cent DDT in alcohol to 6 quarts of water does not affect potability of the water and is effective for 4 to 5 weeks in earthenware jars or wooden barrels where there is no piped water supply. For water not to be used for drinking, either DDT emulsion or Phenothiazine (3 grams per 50 gallons) mixed with a wetting agent (soap, detergents, flour, alcohol) can be used. DDT emulsion can also be applied to the walls of catch basins.

In tropical cities, even where there is no piped water supply, it has been found cheaper, quicker and more completely effective to spray the interior of houses with residual DDT than to use the classical methods of inspection and elimination and treatment of breeding places, for this highly domestic mosquito is particularly susceptible to this technique. This should apply to North American cities as well. Such cities as Georgetown, Barranquilla, and Cartagena have been freed of *Aedes aegypti* within a year.

Mosquitoes and Dengue

Dengue or "breakbone" fever is another virus disease (see p. 233) transmitted principally by mosquitoes of the *Stegomyia* group. The virus is believed to be related to that of yellow fever but differs strikingly in not attacking the liver and in producing immunity of relatively short duration, sometimes only for a season, though some instances of

apparent failure of immunity is undoubtedly due to the existence of at least three different immunological strains. The disease commonly breaks out in explosive epidemics that spread with amazing rapidity. Such an epidemic spread through Texas in 1922; there were estimated to have been 600,000 to 1,000,000 cases in a few months, and 70 per cent of the people in Galveston and Houston were attacked. The disease may occur in all warm parts of the world—north as far as our Gulf states, the Mediterranean countries, and southern China.

The disease starts suddenly with a high fever, flushed face, and severe prostration. Often after a brief let-up there is a return of the fever and a transitory rash. Leucopenia is a marked symptom. The infection is not fatal, but there is a long convalescence. An effective vaccine comparable with that of yellow fever has been developed (Sabin, 1954).

Mosquitoes fed on dengue patients can transmit dengue for 3 days after the onset of the fever. Only *Aedes aegypti* and other members of the *Stegomyia* group are known to be implicated, except a closely related form, *Armigeres obturbans*, in Formosa. In some countries there are dengue-like diseases the transmission of which is uncertain, and it is sometimes difficult to distinguish between true dengue and sandfly fever.

According to the work of Chandler and Rice, *A. aegypti* becomes infected after feeding on patients in the first to fifth days of the disease and can transmit the infection as early as 24 hours after an infective feed, but Siler et al. in the Philippines got different results. They found the patient to be infective for the mosquito for only 3 days, and for 6 to 18 hours prior to the onset, and they also failed to transmit the disease in less than 11 days after a mosquito had obtained an infective feed. This incubation period was later shortened to 8 days by Schule. The only adequate explanation for these discrepant results lies in the possibility of transovarial transmission in mosquitoes and the use by Chandler and Rice of infected stock for breeding experimental mosquitoes. The fact that sandfly fever is transovarially transmitted among sandflies makes it appear probable that this can also occur in the case of dengue and mosquitoes, in spite of some preliminary results to the contrary. The rapid spread of dengue epidemics does not fit in well with a long incubation period in mosquitoes unless hereditary transmission is possible. Once a mosquito becomes infective it appears to remain so for the rest of its life.

Dengue, like yellow fever, is probably a sylvan disease of monkeys, transmitted among them by forest-dwelling mosquitoes of the *Stegomyia* group, such as *Aedes albopictus* and some or all of the seventeen mem-

bers of the *A. scutellaris* group. Human outbreaks presumably begin when some of these mosquitoes become infected from monkeys and then invade human villages where, like *A. aegypti*, they breed in coconut shells and artificial containers. Thence infected human beings carry the disease to other parts of the world where *A. aegypti* takes over as the vector. Monkeys probably serve as inter-epidemic reservoirs of the disease.

A. albopictus is widely distributed in southeast Asia and is one of the four mosquitoes introduced into the Hawaiian Islands; the others are *Aedes aegypti*, *Culex fatigans*, and *Toxorhynchites brevipalpis*, the last being a non-biting species with cannibalistic larvae introduced in 1950 to help make life miserable for *Aedes albopictus*. *A. scutellaris* is found in New Guinea and many other South Pacific Islands. In most Oriental cities *A. aegypti* is the predominant species of the group, but in Honolulu *albopictus* outnumbers *aegypti* three to one, and was the principal vector in the 1943–1945 outbreak there. An interesting feature of the epidemiology of this outbreak was Usinger's (1944) observation that the incidence of cases is correlated with density of human population rather than density of mosquitoes; where people are crowded a few mosquitoes suffice, but where people are scattered even dense hordes of stay-at-home mosquitoes fail to spread the disease efficiently.

Both *A. scutellaris* and *A. albopictus* have a white stripe down the middle of the thorax; *scutellaris* also has two wavy white lines on the sides of the thorax, whereas *albopictus* has irregular white patches instead. Both species have habits very much like those of *aegypti* except that, in addition to breeding in artificial containers, they also breed in axils of leaves and tree holes in jungles far from urban centers and are therefore more difficult to control and probably impossible to exterminate.

For control of *Aedes aegypti* and other container-breeding mosquitoes, see p. 727.

Mosquitoes and Filariasis

Manson's discovery in 1879 that mosquitoes serve as intermediate hosts for filariae marked the beginning of a new era in medical science; it was the first evidence of the development in the bodies of insects of organisms causing human disease. An account of the filarial worms, including the development in mosquitoes, will be found in Chapter 21, pp. 464–473. *Wuchereria bancrofti* and *W. malayi* are the only filarial infections of man known to be transmitted by mosquitoes, though some of the others undergo partial development, up to the "sausage" stage,

in these insects. The species of the genus *Dirofilaria* which inhabit the heart and subcutaneous tissues of dogs are also transmitted by mosquitoes.

Transmitters of *Wuchereria bancrofti*. In contrast to the condition existing in malaria and yellow fever, *W. bancrofti* is not limited to one group of mosquitoes for intermediate hosts, though by no means all species of mosquitoes serve equally well as transmitters. Some fail entirely, some allow only partial development to occur, and some allow only a relatively small percentage of the ingested embryos to reach the infective stage; others, on the other hand, are too hospitable and are frequently killed by the heavy infections which develop; apparently the most critical time for the mosquitoes is during the migration of the matured larvae from breast muscles to proboscis.

Although certain species of all the main groups of mosquitoes serve as intermediate hosts, it is interesting to note that most of the successful "nurses" are the species which are particularly domestic in habit and feed mainly on human blood. The non-periodic *pacifica* form of filariasis of the eastern South Pacific (see p. 466) is transmitted principally by day-biting members of the *Aedes scutellaris* group, particularly *pseudoscutellaris* in Fiji and *polynesiensis* elsewhere. The periodic form, found in all other parts of the world where *W. bancrofti* occurs, is most frequently transmitted in cities by *Culex fatigans* or by the closely related *C. pipiens*, since these mosquitoes are efficient vectors and are abundant. A number of species of *Anopheles* have been found to be better intermediate hosts than these species of *Culex*, and where abundant in small towns or suburbs they undoubtedly play an important role in transmission. This is true of *A. farauti* in New Guinea and the more western Pacific islands, *A. gambiae* and *funestus* in Africa, *A. darlingi* in South America, *A. hyrcanus* in China, and a number of species in India. In Japan *Aedes togoi* has been reported as a transmitter.

Successful transmission of filariae, as of plague, depends on more than mere ability of the insects to allow development of the parasites; some of the cases of frequency of filarial infections in one locality and rarity in another not far distant, with suitable transmitting mosquitoes in both places, have not been satisfactorily explained. Undoubtedly conditions of temperature and humidity are involved. Sundar Rao, in Calcutta, found a distinct seasonal variation in the percentage of infected "wild" mosquitoes (*C. fatigans*) ranging from 3 per cent in July to 12.5 per cent in November and December. Humidity and temperature also influence the successful transfer of larvae to a host when a mosquito harboring them bites.

C. fatigans is the common brown house mosquito of all warm parts of the world. In America it becomes abundant in summer as far north as Washington and St. Louis. It is strictly nocturnal and will bite in complete darkness; therefore its activity supplements that of the yellow-fever mosquito, the house mosquito taking the night shift and the yellow-fever species the day shift. It is probably primarily a molester of birds, attacking man and other mammals as a second choice. It breeds in almost any standing water but prefers artificial containers and is partial to filthy water. It thrives in cesspools and open sewers. The larvae (Fig. 231) have long breathing tubes and broad heads. Development from egg to adult can probably occur in 5 or 6 days under ideal conditions.

Transmitters of *Wuchereria malayi*. The form of filariasis caused by *Wuchereria malayi*, in contrast to *W. bancrofti* infections in most places, is strictly rural, because it is transmitted, exclusively or nearly so, by mosquitoes of the genus *Mansonia*. In India and Ceylon *M. annulifera* is the most important species, but in Malaya and the East Indian Islands several other species are involved (see p. 473).

Mosquitoes of the genus *Mansonia* differ from all others in their biology. The eggs of the tropical species are laid in clusters on the under surface of leaves of aquatic plants. The larvae have the breathing tube terminated by a spine (Fig. 235, 11) with which they pierce the roots of the plants and draw air from them and so never come to the surface. The pupae use their breathing trumpets in a similar manner, and they, too, never rise to the surface until time of emergence.

Most of the species are found in the tropics. Some, including the important *malayi*-carrier in India, *M. annulifera*, are closely associated with the water lettuce, *Pistia stratiotes*, that grows extensively in tropical swamps. Iyengar in 1938 was able to control *malayi* infection in India by raking up and destroying this plant. Another vector, *M. uniformis*, chooses the water hyacinth, and in parts of China and Indo-China *M. longipalpis* attaches itself to the roots of many plants, including swamp trees; this species is very difficult to control.

Mosquitoes and Encephalitis

In nearly all parts of the world there occur arthropod-borne filtrable viruses which are at least potentially neurotropic, and capable of causing encephalitis or encephalomyelitis in man or animals. Many varieties or strains have been isolated which differ among themselves in their antigenic characters and to some extent in their vectors, pathogenic propensities, and host preferences. Some cause extensive epidemics

among horses or other animals, or even among human beings; some have been discovered by isolation from the blood of normal or febrile man or animals, and some have thus far been isolated only from mosquitoes, causing encephalitis when inoculated into laboratory animals. Some of the viruses considered elsewhere, e.g., yellow fever (p. 720), dengue (p. 727), sandfly fever (p. 652), Colorado tick fever (p. 577), spring-summer encephalitis (p. 577), and louping ill (p. 577) also belong to or are related to this group.

Three arthropod-borne encephalitis viruses occur in the United States—western equine, eastern equine, and St. Louis. Horses suffer severely from the eastern and western equine strains but have only inapparent infections from the St. Louis strain, as indicated by development of virus-neutralizing antibodies. Many other mammals and particularly wild and domestic birds develop mostly inapparent infections and are undoubtedly important reservoirs of these infections. Human infections are not frequent enough to constitute an important public health problem except rarely. There have been three rather serious human outbreaks of western equine, and the St. Louis virus caused over 1000 cases in that city in 1933, but eastern equine has caused only sporadic human cases, even after extensive epizootics among horses, pheasants, etc.

The disease comes on suddenly with malaise and intense headache; a continued fever reaches its peak on the third day and then gradually subsides, and there is marked drowsiness or coma. Nausea, vomiting, and convulsions are common. The fatality is 3 to 22 per cent in different outbreaks and is higher in adults. Human cases are often preceded by horse epizootics; they occur most commonly in rural, irrigated areas. The disease reaches a peak in midsummer and spreads in an erratic manner.

Although numerous culicine mosquitoes have been shown to be capable of harboring and transmitting these viruses in the United States, *Culex tarsalis* is the most important vector of both western equine and St. Louis viruses in the west. This mosquito is easily distinguished from other species of *Culex* by its striped legs, band on proboscis, and dark v-shaped spots on the underside of the abdomen. It shows little choosiness as to breeding places, and breeds in great numbers in irrigation seepage or overflow, rice fields, etc. *C. fatigans* was probably the principal vector of St. Louis virus in the 1933 outbreak. For eastern equine, *Culex pipiens* is probably an important vector, but other culicines, especially *Aedes vexans*, and species of *Psorophora*, *Mansonia*, and *Theobaldia* are also involved.

A Venezuelan strain has been found in Trinidad, Venezuela, and

Ecuador, with *Culex fatigans* and *Aedes taeniorhynchus* among possible transmitters. An equine and human outbreak in Trinidad suggested introduction by salt marsh mosquitoes from the Venezuelan coast. In Colombia and Brazil several strains of viruses in addition to jungle yellow fever have been isolated from forest mosquitoes. In the Far East, from Guam and the Philippines to Japan, Korea, and Manchuria, Japanese B virus is present, transmitted primarily by *Culex tritaeniorhynchus*, although *C. fatigans*, *C. annulirostris*, and some species of *Aedes* and *Anopheles* are also involved. *Aedes chemulpoensis* is an important vector in North China. Infection, as indicated by antibodies, is common in mammals but much less common in birds, probably because *C. tritaeniorhynchus*, unlike *pipiens*, feeds more on mammals than on birds. There have been some extensive human epidemics. In Australia, Murray Valley virus affects many birds and mammals, and causes some human cases. It seems to be endemic in Queensland, in favorable seasons being carried by birds to southern parts of Australia.

In Africa virologists hit the jackpot in unearthing, to date, nearly a dozen distinct strains of virus, all of which are probably infective for man. In 297 human sera examined in a locality in East Africa, neutralizing antibodies against eight different viruses were found, only 17 per cent being negative. One virus (Bwamba) was present in 44 per cent, and another, Zika, was associated with an outbreak of jaundice. Two of these African viruses which were thought to be rare in man (West Nile and Ntaya) have been shown to be extremely common in Egypt, where over 50 per cent of children show antibodies to West Nile virus by the time they are 5 years old, and 75 per cent of adults show them. Over 45 per cent of adults show antibodies to Ntaya virus. West Nile antibodies are also common in domestic animals and wild and domestic birds, and this virus has also been found in man in Israel.

In Egypt species of *Culex* have been shown to be naturally infected, and *Aedes aegypti* is an experimental vector. Transmission occurs from the sixth day on, but there is no transovarial transmission. Little is known about the pathogenicity of these viruses in infants; in inoculated adults they produce mild fever, and in only about 10 per cent temporary symptoms of encephalitis such as drowsiness, muscle twitching, etc. In an accidental laboratory infection malaise and muscle pains were complained of. Another of the African viruses, Rift Valley, is particularly harmful to sheep and cattle, is deadly to small rodents, and sometimes produces dengue-like attacks in man. Mosquitoes involved are various species of *Aedes* and *Eretmopodites*. Another

virus, Mengo, has been found in four continents but seems nowhere to be prevalent.

There has been such speculation as to how these encephalitic viruses survive in countries with cold winters, since they do not appear to survive in either mosquitoes or in the vertebrate hosts. What becomes of them in inter-epidemic periods? When it was found that a high percentage of birds show antibodies and that their bloodsucking dermanyssid mites harbor the infection, and especially when it was reported that the St. Louis virus could be transmitted by the mites to their hosts and also transovarially to their offspring, this appeared to provide a good explanation. The mites are the reservoirs, they infect non-immune nestling birds, mosquitoes bite the birds and transmit the infection to other birds, and in a seasonally dead-end sidetrack to horses and man. But repeated attempts to confirm this work have failed and the role of mites in the epidemiology of the disease is a controversial subject. The birds are infected and the mites are infected, but *transmission* does not commonly occur (see Eklund, 1954, in References, Chap. 23).

Another suggestion is that the viruses are permanently at home only in warm countries, and may be annually reintroduced by migratory birds. Eklund called attention to another interesting phenomenon: the temperate-climate viruses are transmitted principally by *Culex*, which are primarily bird-biters, the tropical ones by *Aedes*, *Haemagogus*, etc., which are primarily mammal-biters. The only bit of evidence in support of the migratory bird theory is in connection with the extension of Murray Valley virus from tropical Queensland to temperate southern Australia in favorable seasons.

Mosquitoes and *Dermatobia*

In many parts of tropical America where the larva of a botfly, *Dermatobia hominis* (see p. 760), infests man and cattle, there has long been a belief among the natives that the maggots which develop under the skin result from mosquito bites. Observations and experiments proved this to be true; mosquitoes normally serve as airplanes for the transportation of *Dermatobia* eggs to a suitable host. Occasionally when a *Dermatobia* is unable to find a mosquito and is under the immediate necessity of depositing eggs, she may oviposit on other captured arthropods or even on leaves.

The mosquitoes involved in nature seem to be, primarily at least, species of *Psorophora*, subgenus *Janthinosoma*. In Central America *P. luzii* alone has been incriminated, but in South America other species are concerned; *P. ferox* is the most frequent vector in Colombia.

P. lutzii (Fig. 243) is a dark, beautifully colored mosquito, with yellow markings on the thorax and with flashes of metallic violet and sky blue on its thorax and abdomen. It is said by Knab to be one of the most bloodthirsty of American mosquitoes and is found throughout tropical America. The larvae breed in rain puddles, the eggs being

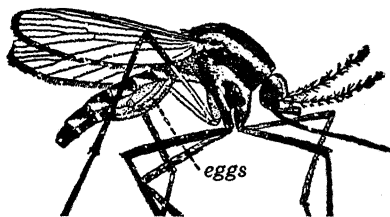


FIG. 243. *Psorophora (Janthinosoma) lutzii*, with eggs of *Dermotobia hominis* attached to abdomen. (After Sambon, *J. Trop. Med. Hyg.*, 25, 1922.)

laid in dry depressions on the forest floor which will become basins of water after a tropical downpour. The eggs hatch almost with the first drop of rain and mature so rapidly that adult insects may emerge in 4 or 5 days. The larvae feed on vegetable matter and are themselves fed upon by their relatives of the subgenus *Psorophora*, which breed in the same rain pools.

Control and Extermination

Control or protection against mosquitoes and mosquito-borne diseases may be undertaken in the following ways: (1) personal protection from adults, (2) destruction of adults, (3) destruction of larvae, and (4) elimination of breeding places.

Personal Protection. This method of dealing with mosquitoes may be indispensable to people operating in mosquito-infested places and for residents in some areas, as in parts of Alaska where control methods are unpracticable. Concerning the use of protective clothing, little need be said; the value of gloves, veils, high boots, leggings, etc., is obvious. There are a number of repellents now available which give protection for several hours, not only against mosquitoes but against other pests as well, such as blackflies, deerflies, mites, etc. These are discussed on p. 519. In many parts of Alaska protection against mosquitoes outdoors is essential for playing children, etc., and is obtained by more or less stationary aerosol dispensers situated so the insecticidal mist will drift over the areas to be protected. Similar protection is obtained in some cities by mists dispensed from trucks moving up and

down the streets, or locally for protection of outdoor gatherings. Indoor protection is obtained by means of screens; their effectiveness is enhanced by spraying them with residual insecticides so that fewer will enter when doors are opened. Residual sprays indoors (see below) make screens less essential in some places, but they are still valuable against light-attracted insects at night and for protection against DDT-resistant flies.

Destruction of Adults. Immediate destruction of mosquitoes and other insects in houses, barracks, schools, etc., can be obtained by the use of aerosol "bombs" (see p. 517). For continued protection, however, residual sprays with DDT or other chlorinated hydrocarbons in suspensions or emulsions, at the rate of 200 mg. per square foot of the insecticide, are needed. The surfaces sprayed are lethal for 3 to 6 or 8 months to insects resting on them, depending on the nature of the surface, formulation of spray, etc. For details, see p. 517.

Residual spraying of houses has given sensational success against insect annoyance and in control of arthropod-borne diseases wherever the vectors habitually enter houses and rest in them. As noted on p. 727, this method may actually exterminate the domestic *Aedes aegypti*, and it gives such excellent protection against house-frequenting *Anopheles* (e.g., *A. darlingi*, *A. quadrimaculatus*, *A. gambiae*) that malaria is quickly reduced to a position of minor importance, or eliminated altogether (see pp. 208-209). On the other hand, residual spraying is of little or no use against the mosquitoes that bite only outdoors, or leave a house immediately after feeding. This includes members of the *Aedes scutellaris* complex, which are important vectors of filariasis and dengue in the Pacific area, and also such *Anopheles* as *A. bellator* and to some extent *A. albimanus* and *A. aquasalis*. Unfortunately insects are adaptive creatures, and we must contemplate three possibilities: (1) that some of the house-frequenting species may develop bite-and-run habits as a result of natural selection and survival of the fleetest, just as they once substituted domesticity for a sylvan life before human houses were converted into lethal traps; (2) that some of the present bite-and-run species, when their house-frequenting competitors are eliminated, may become of greater importance; and (3) that mosquitoes may in time become as resistant to DDT and allied chemicals as have flies. Up to the present time only a few species of *Anopheles* have developed any appreciable degree of resistance, and only locally, but several others, (*Culex tarsalis* and the salt marsh mosquitoes, *Aedes sollicitans* and *A. taeniorhynchus*) have become fairly resistant in some places.

A novel method of killing adult male mosquitoes is the use of a

loud-speaker set up behind an electrified screen to broadcast the sounds made by the female of the species (Kahn and Offenhauser, 1949).

Many birds, especially nighthawks, swifts, and swallows, feed actively on adult mosquitoes. Bats have been exploited as mosquito destroyers, and municipal bat roosts have actually been erected in San Antonio and recommended for other places, but scientific investigation has not substantiated the extravagant claims made for the efficiency of bats as mosquito destroyers. In the tropics wall lizards or geckos and jumping spiders destroy numbers of mosquitoes in dwellings.

Destruction of Larvae. The classical methods of destroying mosquito larvae in their breeding places have been (1) oiling, (2) application of emulsified larvicides, (3) Paris green dusting (for *Anopheles* only), (4) clearing of brush and floating vegetation to permit fish, particularly *Gambusia*, to reach the larvae and devour them, and (5) fluctuation of water level. The last has been very helpful in preventing breeding in reservoirs. When the level is lowered, great numbers of larvae are stranded and die; when it is raised, fish can get access to larvae that were developing near the lower shore line.

The choice of larvicidal measures depends, of course, on local conditions. The first three methods mentioned above have been largely superseded by spraying with DDT or other chlorinated hydrocarbons (for details see p. 518). *Anopheles* larvae are so susceptible to DDT that, if evenly distributed, 1 lb. of DDT would be enough to kill them on 1000 acres; in practice 100 times that amount is used. No harmful effects on fish or other wildlife results from such dosage. In rice fields heavy dusting before flooding greatly retards mosquito breeding. One-inch cubes of plaster of Paris and sawdust soaked in a 5 per cent solution of DDT suppresses breeding in wells for several weeks.

In treating catch basins, cesspools, sewer inlets, etc., a residual effect good for several months can be obtained by spraying the side walls. For a sewage farm, application of 8 oz. of a 25 per cent emulsion every day or two to the water in the main pipeline did the work of spraying 75 to 100 gallons of diesel oil. By treating a main irrigation ditch with a few gallons of emulsion applied slowly over a period of an hour or so, larvae can be killed for distances of many miles; in one case no larvae were found in 100 miles of irrigation canals.

Natural Enemies. Certain kinds of fish are of very great value in control of mosquito larvae in natural waters, lily ponds, etc. The viviparous *Gambusia affinis* (Fig. 244), widely distributed in southeastern United States and extensively introduced elsewhere, is a valuable species because of its hardiness, ability to live in fresh, brackish, or foul water, and rapid multiplication.

Where algae, weeds and debris are removed to permit free operation of the fish, usually no other control is necessary. Even goldfish may keep lily ponds free if the mosquitoes do not breed more rapidly than the fish can eat them. In salt marshes, various species of killifish (*Fundulus*) are potent factors in destroying mosquito larvae. Great

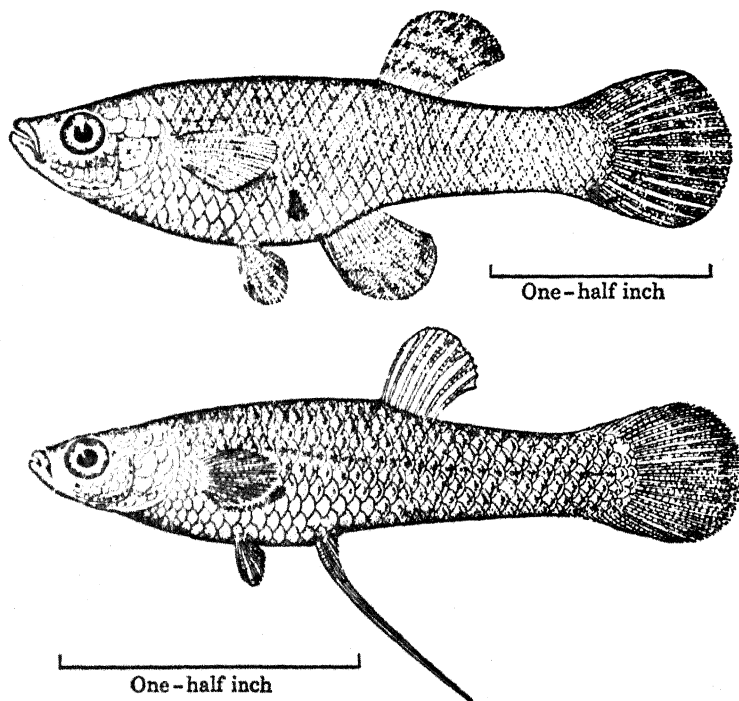


FIG. 244. *Gambusia affinis*, a voracious, mosquito-eating top minnow, useful for stocking ponds, cisterns, wells, etc. (After Jordan and Evermann, *The Fishes of North and Middle America*.)

reduction in mosquito output can be obtained by draining marshes in such a way that the fish can get access to most parts of them. If swamps are converted into pools in their deepest parts, fish can sometimes control the mosquito output. *Gambusia* can be used to advantage in cisterns and exposed wells. Many southern cities have hatcheries for these fish to supply them to citizens who have use for them.

Other natural enemies such as newts can sometimes be exploited in a similar manner. Many other water inhabitants attack mosquito larvae or eggs, including predaceous insects, bugs, mites, etc., so it is not desirable, when it can be avoided, to kill such life while attempting to kill mosquito larvae. A number of aquatic plants are inimical to

mosquito larvae for one reason or another, *Chara* apparently by producing a high oxygen content of the water, the bladderwort, *Utricularia* by capturing the larvae in its trap-like bladders, and surface-covering plants such as *Lemna* (duckweed) by preventing the larvae from getting access to air.

Elimination of Breeding Places. The only permanent method of control of most mosquitoes is to eliminate the breeding places entirely wherever possible. The application of this method to container-breeding mosquitoes was discussed on p. 727.

Drainage is often practicable as a means of eliminating breeding places. Not only must small pools of standing water be eliminated but also the drains themselves must be made unsuitable for breeding. Sometimes other methods of control, such as filling in of depressions or protection of swamps by means of levees, dikes, or tide gates are more practicable. Drainage ditches with narrow bottoms, the sides of which are kept clean and straight, preferably by cement or board walls, are the best means of draining borrow pits, swampy depressions in streams, or outcrops of seepage water. Seepage water outcrops are the most difficult and often have to be drained by ditches which more or less follow the contours, ultimately connecting with main ditches leading away. Lined ditches cost more to build but are more permanent, more easily kept clean, and cheaper in the long run.

Subsoil drainage by means of tile or pipe is often necessary; in the Malayan hills Watson got wonderful results by thus draining ravines where *A. maculatus* breeds, and excellent results have been obtained from this method in Panama also. In some places effective drainage has been obtained by packing drains or tributaries of ravines with tree trunks and branches and a top covering of grass. Where water is held at the surface by an impervious stratum overlying a pervious one vertical drainage may be successful, by drilling holes through which the water can flow down to the deeper pervious strata. Salt marshes may be drained by appropriately placed drains averaging 200 to 300 ft. to the acre, the method successfully used by Headlee in New Jersey, with filling in of parts which cannot be so drained; the falling of the tide carries the water out of the ditches. When the tide is insufficient to do this, engineering projects of diking with tide gates or pumps must be resorted to. In some places dams and automatic siphons, to flush streams in the dry season when pools form in their beds, have been found useful.

Periodic draining of ponds and rice fields results in a great reduction in number of *Anopheles* larvae. In California 10-day intervals between drying have been employed, and in Portugal 16 days. Sometimes pro-

vision of shade, sometimes removal of it, eliminates breeding places (see p. 717). For bromeliad-breeding species of *Anopheles* (*A. bel-lator*, *A. cruzi*) spraying with 0.5 per cent copper sulfate kills the plants, but in some places hand removal of them is preferable. In either case not *all* the aerial plants need be removed, for some of the smaller species, which are often the most inaccessible, are of little or no importance. Once eliminated there may be no regeneration of the plants for 10 years or more.

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Diptera

III. Fly Maggots
and Myiasis

Disgusting as it may seem, man and animals are attacked not only by the numerous adult flies discussed in the last two chapters but also by the maggots or larval stages of many species of flies. Such an infestation by fly maggots is called myiasis. Nearly all cases are caused by larvae of flies of the suborder Cyclorrhapha (see p. 646). Exceptions are a few reported cases of infestation of the skin by a scale insect; of sinuses by the larvae of carpet beetles; and of the rectum by adult dung beetles. The last, and many other unusual cases of beetles or maggots in the feces, stomach, urinary passages, nose, etc., are clearly accidental causes of pseudoparasitism (see Théodorides, 1948). Mention should also be made of dermatitis produced by products of non-parasitic insects, especially the blisters formed by tiny beetles of the genera *Paederus* (a staphylinid) and *Epicauta* (a cantharid), and the great irritation produced by the poison hairs of a caterpillar, *Megalopyge opercularis*, popularly called an "asp."

The flies most frequently concerned in myiasis belong to two large groups, the Muscoidea (see p. 671) and the botflies. The latter are committed to parasitic life in the larval stage, and live for a very short time, probably not feeding at all, in the adult stage. Their mouth parts are reduced to mere vestiges. Many of the Muscoidea, on the other hand, are a nuisance in the adult stage as bloodsuckers or germ carriers, but some, such as the screwworms and the African tumbu fly, have to be reckoned with as important parasites in the larval stage, and a few, such as the housefly, may cause trouble in *both* stages. Many Muscoidea belonging to the families Calliphoridae and Sarcophagidae, commonly called blowflies or fleshflies, have maggots that feed on dead flesh, and it is not surprising that some of these should have adapted themselves to entering wounds and feeding on living flesh, e.g., the screwworms, or to developing in the foul-smelling soiled wool of sheep and attacking the skin underneath, e.g., the wool maggots.

Identification. Identification of full-grown larvae causing myiasis is usually not difficult so far as the genera are concerned, but accurate determination of species often requires breeding them out. The most important characteristics used for identification are the respiratory openings at the anterior and posterior ends of the abdomen (Fig. 246). The posterior openings consist of two stigmal plates; these are hardened, dark-colored, eye-like spots, in most species surrounded by a chitinized ring and a button-like mark, though in some of the Oestridae the whole plate is chitinized. On the plates the spiracular openings are usually in the form of three slits, which may be straight, bent, or looped. The position and shape of the plates, the development of the ring and button, and the form of the slits are of great value in identification.

First-stage maggots are recognizable as such by the absence of anterior spiracles and posterior spiracular plates, but the genera and species are difficult to identify. Second-stage maggots are also difficult to identify; in the muscoid group they are recognizable as such by the presence of two instead of three spiracular slits.

Following are keys to the principal myiasis-producing adult flies and their larvae, including a few forms most likely to be confused with them, but not including adults of those only occasionally found in human feces.

Adult Myiasis-Producing Flies

- I. **Muscoidea** (Muscidae, Calliphoridae, and Sarcophagidae). Eyes large (Fig. 247), touching or nearly so in ♂; proboscis well developed.
 - 1a. Color metallic blue or green; **Calliphoridae** 2.
 - 1b. Color gray or yellowish with dark markings 4.
 - 1c. Color yellowish brown; **African Calliphoridae** 5.
 - 2a. Bristles on mesonotum mostly wanting (Fig. 245, 2); blue or greenish blue; face golden or orange-red; palpi short; antennae feathered to tip (Fig. 245, 5) **Callitroga** and in Old World, **Chrysomyia**. 3.
 - 2b. Bristles well developed on mesonotum (Fig. 245, 1) 3.
 - 3a. Small; green or coppery; face silver; alulae bare (Fig. 245, 1) **Phoenicia**.
 - 3b. Large; blue; face red or golden; alulae hairy **Calliphora**.
 - 3c. Larger; bluish black; face black **Phormia**.
 - 4a. Abdomen yellowish basally, dark at apex, with longitudinal dark stripe; proboscis fleshy **Musca**.
 - (1) Similar but more slender; fourth wing vein straight, not curving up towards third (Fig. 245, 7) **Fannia**.
 - 4b. Abdomen checkered gray and black; arista feathered except at tip (Fig. 245, 4) **Sarcophaga**.
 - 4c. Abdomen gray spotted with black; arista bare (Fig. 245, 3) **Wohlfartia**.
 - 5a. Abdominal segments all about equal (Fig. 249) **Cordylobia**.
 - 5b. Second abdominal segment of ♂ elongated (Fig. 247); third abdominal segment of ♀ indented **Aucheromyia**.
- II. **Botfly Group** (Gastrophilidae, Cuterebridae, and Oestridae). Eyes

small, widely separated (Figs. 255, 256); proboscis greatly reduced or absent.

- 1a. Body not markedly hairy; proboscis small, in pit; arista feathered on one side *Cuterebridae*.
 (1) Body blue, wings brown; tropical American skin maggot of cattle and man (Fig. 255) *Dermatobia*.
 (2) Body moderately hairy, black and white; anal vein poorly developed; skin maggots of rodents and cats *Cuterebra*.
 1b. Body hairy, bee-like 2.

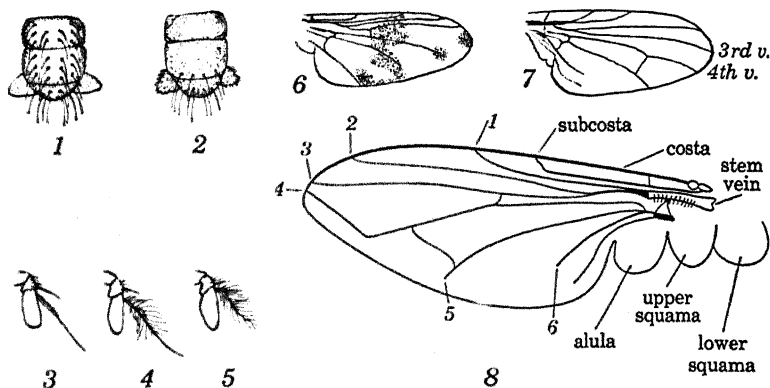


FIG. 245. Details of structure of myiasis-producing flies to illustrate key. 1, Thorax of a *Lucilia*, dorsal view, showing well-developed bristles in median two rows of mesonotum, and hairless alulae. 2, Thorax of *Callitroga hominivorax*, dorsal view, showing absence of bristles in median two rows except at hind end of mesonotum, and hairy alulae. 3, Antenna of *Wohlfartia*, with naked arista. 4, Antenna of *Sarcophaga*, with arista feathered on basal half. 5, Antenna of *Callitroga*, with arista feathered to tip. 6, Wing of *Gastrophilus intestinalis*, showing straight fourth vein not reaching margin, and spotting of wing. 7, Wing of *Fannia*, showing straight fourth vein. 8, Wing of a typical muscoid fly, showing veins (with numbers), alula, and squamae.

- 2a. Abdomen elongated; fourth vein of wing straight, not extending to margin of wing (Fig. 245, 6) (horse bots) *Gastrophilidae*.
 (1) Abdomen brown, tipped with red (Fig. 257, 4) *Gastrophilus haemorrhoidalis*.
 (2) Abdomen light at each end with black band in middle; wings not spotted *Gastrophilus nasalis*.
 (3) Abdomen brown, dirty white at base; wings spotted (Fig. 245, 6) *Gastrophilus intestinalis*.
 2b. Abdomen short, rounded; fourth vein of wing curved forward at tip, sometimes closing first posterior cell (Fig. 256); mouth parts vestigial; arista bare; *Oestridae* 3.
 3a. Middle part of face narrow; color dirty or grayish *Oestrus*.
 3b. Middle part of face broad; color mainly blackish *Hypoderma*.
 (1) Apex of abdomen orange; thorax not distinctly striped *H. bovis*.
 (2) Apex of abdomen lemon-yellow; light lines on thorax *H. lineata*.

Full-Grown Larvae of Myiasis-Producing Flies

- I. Larvae cylindrical, tapering anteriorly (Figs. 217, 248); fairly smooth, without conspicuous colored spines; skin not leathery; stigmal plates separated, well chitinized, with 3 spiracular slits (*Muscoidea*).
 - 1a. Chitinous ring completely encircles plate; button well developed 2.
 - 1b. Chitinous ring incomplete; button region poorly chitinized 5.
 - 2a. Two mouth hooks; slits straight, or oval and only slightly bent 3.
 - 2b. One mouth hook; slits S-shaped or in loops 4.
 - 3a. Button enclosed in ring; slits straight, elongate, directed inward and downward (often nearly horizontal in *Calliphora*) (Fig. 246) *Calliphora*, *Lucilia*, and *Phoenicia*.
 - 3b. Button inside ring; slits oval, may be slightly bent *Muscina*.
 - 4a. Slits have several loops; stigmal plates D-shaped, close together (Fig. 246) *Musca*.
 - 4b. Slits S-shaped and well separated; stigmal plates separated by nearly twice their diameter (Fig. 246) *Stomoxys*.
 - 5a. Stigmata in pits surrounded by fleshy tubercles (Fig. 251); slits vertical, the first one often directed downward and outward *Sarcophagidae*.
 - 5b. Stigmata not in pits 6.
 - 6a. Large break in ring; no definite button (Fig. 246); posterior margin of eleventh segment without dorsal spines *Callitroga*.
 - (1) Main tracheae large, pigmented (Fig. 248) *C. hominivorax*.
 - (2) Main tracheae small, not pigmented (Fig. 248) *C. macellaria*.
 - 6b. Ring often nearly complete, but no definite button *Chrysomya*.
 - 6c. A weakly chitinized button present. *Phornia*; in birds' nests. *Apaolina*.
- II. Larvae leathery, usually more or less flattened, not tapering from posterior to anterior end; often with conspicuous, colored spines (bots).
 - 1a. Body with rings of large, dark spines (Fig. 257, 5); stigmal plates in contact, each with 3 bent slits (Fig. 246) (horse bots). *Gastrophilus*.
 - 1b. Body entirely covered with black spines; stigmal plates with 3 convoluted spiracles spread laterally, converging medially to lower inner angle; in skin of rodents and cats *Cuterebra*.
 - 1c. Body not as above 2.
 - 2a. Stigmal plates with 3 slits in each 3.
 - 2b. Stigmal plates solid, with numerous small openings 5.
 - 3a. Body with last segment retractile; anterior end large; cuticle sparsely studded with dark spines (Fig. 255); stigmal plates close together; slits slightly bent (tropical American skin maggot) (Fig. 246) *Dermatobia*.
 - 3b. Stigmal plates well separated 4.
 - 4a. Plates very poorly developed, less than their own width apart, the slits crooked (Fig. 246); body studded with small yellow spines (African skin maggot) *Cordylobia*.
 - 4b. Plates small, very far apart, the slits horizontal (Fig. 246); rings of small spines on body (African bloodsucking maggot) *Aucheromyia*.
 - 5a. Button well inside plate (Fig. 246); body with rows of strong spines on ventral side; in nostrils and other parts of head of sheep *Oestrus*.
 - 5b. Button on inner margin of plate; in nostrils of horses *Rhinoestrus*.
 - 5c. Button in median indentation of plate (Fig. 246); no conspicuous spines; in skin of cattle (Fig. 256) *Hypoderma*.

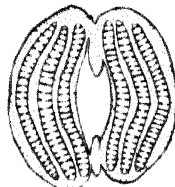
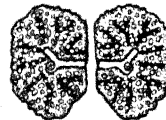
*Aucheromyia luteola**Cordylobia anthropophaga**Stomoxys calcitrans**Musca domestica**Calliphora vomitoria**Phoenicia caesar**Wohlfartia vigil**Callitroga macellaria**Hypoderma lineata**Gastrophilus sp.**Hypoderma bovis**Dermatobia hominis**Oestrus ovis*

FIG. 246. Stigmal plates and spiracles of various maggots. Note distance apart of stigmal plates, form and position of spiracles, and presence or absence of "button." (Adapted from various authors.)

- (1) Plates kidney-shaped (Fig. 246); no spines on last segment *H. lineata*.
 (2) Plates deeply indented; no spines on last 2 segments *H. bovis*.
 III. Larvae of odd types occasionally found in feces.
 1. Large, flat, dark-colored, 11-segmented, with distinct head (a member of the soldier-fly family, Stratiomyidae) (Fig. 252D) *Hermetia illucens*.
 2. Cylindrical, with long tail-like process (rat-tailed maggot, member of family Syrphidae) (Fig. 252C) *Eristalis*.
 3. Small larvae with spiracles on tubercles; acalyptrate flies of families Piophilidae, Drosophilidae, etc. (cheese skippers, fruit flies, etc.) (Fig. 252B).
 4. Flattened, with fleshy processes (Fig. 252E) *Fannia*.

Types of Myiasis. Maggots attack their hosts in a number of different ways. The Muscoidea group includes maggots that (1) suck blood; (2) invade wounds and natural cavities (nose, ear, etc.); (3) attack skin under soiled wool, causing "strike" in sheep; (4) live in boils under the skin; and (5) live in or pass through the intestine or urinary tract. The botfly group includes species that (1) live in boil-like lesions in the skin; (2) cause warbles in the skin of cattle; (3) attack the nasal passages, sinuses, or other parts of the head of domestic animals or deer; and (4) live in the stomach or rectum of horses. Each of these will be briefly considered below.

MUSCOID MAGGOTS

1. Bloodsucking Maggots

A number of species of flies allied to the blowflies deposit their offspring in the nests of birds, where the maggots attach themselves to the nestlings and suck blood. In northern United States and Canada, species of *Apaulina*, and in the Old World, *Protocalliphora*, have this habit. Hole-nesting passerine birds and hawks suffer most.

The only larva that sucks blood by puncturing the skin of man is the Congo floor maggot, *Aucheromyia luteola*, found throughout tropical Africa south of the Sahara Desert, wherever there is a "stay-put" population of people who sleep on mats on the floor. Where the people are nomadic or sleep on raised beds, this parasite cannot hope to survive. It is the only known fly that is exclusively parasitic on man. Even where man and animals sleep in the same room, the maggots are found in the sand or dust only where human beings have lain. The adults commonly rest on walls indoors and feed by preference on human feces, though also attracted to fermenting or decaying vegetation found far from human dwellings. Other species of this genus and the related

genus *Choeromyia* live in the burrows of the wart hog and other hairless mammals.

The adult fly (Fig. 247A) is a dirty yellowish brown with the tip of the abdomen rusty black; it resembles *Cordylobia* in general appearance (see key, p. 743, and cf. Fig. 249). The female lays her eggs in

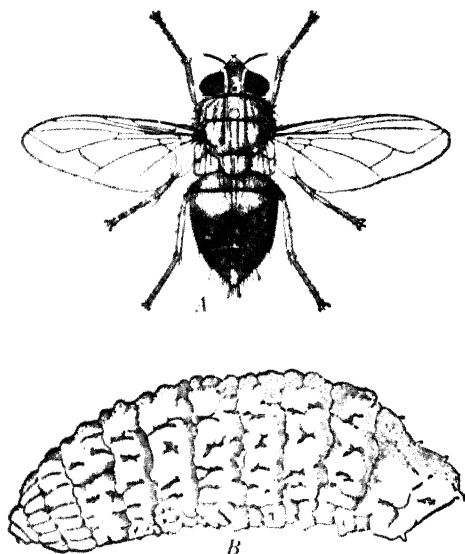


FIG. 247. Congo floor maggot and adult fly, *Aucheromyia luteola*. A, $\times 3$; B, $\times 4$. (Adult after Manson-Bahr, *Manson's Tropical Diseases*, Williams and Wilkins; larva after James, *U. S. Dept. Agric. Misc. Publ.* 631, 1947.)

batches of about 50 at a time, usually in dust along the edges of sleeping mats; she may have 5 or 6 egg-laying sessions at intervals of a week or so. The eggs hatch within 2 days, and a few hours later the larvae are ready to suck blood, although if the occupant of the sleeping mat happens to be off on a vacation they can live unfed even for several weeks. The larvae (Fig. 247B) feed several times between molts, pupate after several weeks, and the adults emerge 10 days or so later. The life cycle probably occupies about 10 weeks, so there could be five generations in a year (Garrett-Jones, 1951). The larvae lie buried in dust under the floor mats in the daytime and come forth every night to pierce the skin with their mouth hooks and suck blood. For most people the bites are not very irritating, and there is no record of their transmitting disease.

2. Myiasis of Wounds and Natural Cavities (Screwworms)

Secondary Invaders. A large number of flies belonging to the muscoid group, which normally deposit their larvae in decaying flesh of dead animals, occasionally, probably more or less by accident, deposit their eggs or larvae in neglected wounds or sores when offensive discharges are exuding from them. Included in this group are many blue, green, or coppery-colored species of Calliphoridae belonging to the genera *Calliphora*, *Phoenicia*, *Phormia*, *Callitroga*, *Chrysomyia*, and others, and gray and black Sarcophagidae of the genera *Sarcophaga* and *Wohlfartia* (see key on p. 743). There are, however, a small number of species which are commonly found as secondary invaders of wounds. These include *Callitroga macellaria*, *Phormia regina*, several species of *Phoenicia* and *Lucilia*, and one or two species of *Sarcophaga* (see Fig. 253) in this country, and *Chrysomyia megacephala* and others of this genus in the Old World. Some species deposit their eggs in befouled wool of sheep and later invade the body (see p. 754).

The secondary invaders are not primarily attracted by living tissue but only by decomposed tissue such as would be found in a dead animal. For this reason, and because their excretions have bactericidal properties, some of them were extensively used as a means of removal of dead tissue in cases of osteomyelitis, before the advent of antibiotics. The maggots would, however, attack healthy living tissue when dead tissue was not available, as Stewart demonstrated in 1934 in the case of the supposedly exclusively saprophagous *Phoenicia sericata*, which has been widely used as a "surgical maggot."

Primary Invaders (Screwworms). Of far greater significance are three species which deposit their eggs on fresh wounds of living animals and feed primarily upon the living tissues. They do not deposit their eggs on the unbroken skin but require only an insignificant wound or scratch, very often a tick bite. Apparently the odor of fresh blood is attractive to them. They are also attracted by the odors emanating from diseased natural cavities of the body and may oviposit in the external ear, mouth, nose, eye, or vagina, whence they penetrate to the middle ear, sinuses, or other parts of the body. Severe infestations in man may lead to a loathsome and horrible death.

As already noted only three species of flies are known normally to attack living animals in this manner and to feed on living flesh. These are the American screwworm fly, *Callitroga hominivorax*; the Old World screwworm, *Chrysomyia bezziana* of southern Asia and South Africa; and *Wohlfartia magnifica* of eastern Europe.

CALLITROGA HOMINIVORAX. This highly injurious fly, formerly placed in the genus *Cochliomyia*, and long known as *Callitroga* (or *Cochliomyia*) *americana*, was confused with a closely related carrion-feeding species, *C. macellaria*, until Cushing and Patton differentiated

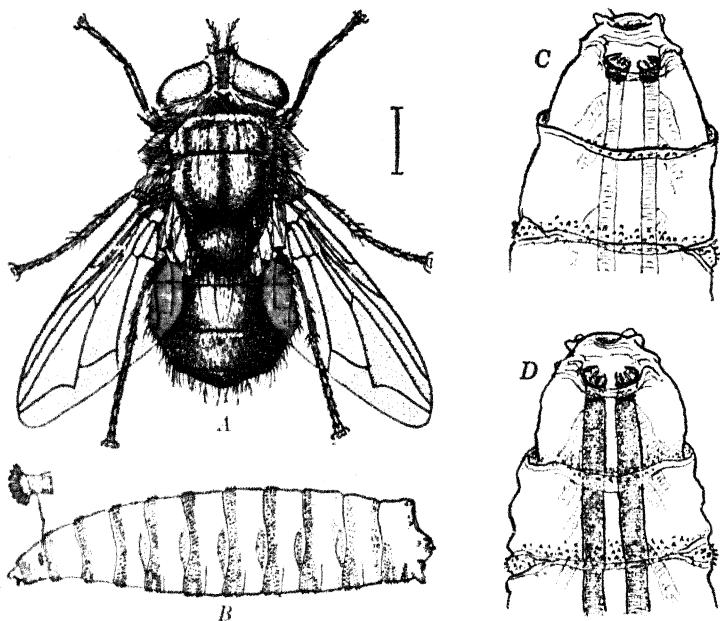


FIG. 248. A, Screwworm fly, *Callitroga hominivorax* adult ♀; B, full-grown (third stage) larva, anterior spiracles shown separately, enlarged. (Adult after James; larva after Lauke, Cushing and Parish, from James, *U. S. Dept. Agric. Misc. Publ.* 631, 1947). C, posterior end of *C. macellaria*, ventral view. D, same of *C. hominivorax*. Note large, heavily chitinized, dark tracheae of *C. hominivorax* and small, lightly chitinized, uncolored tracheae of *C. macellaria*.

them in 1933. The adult flies of these two species are very difficult to distinguish, but the maggots show easily recognizable differences (see key, p. 745, and Fig. 248C).

C. macellaria breeds in carcasses and only secondarily invades foul-smelling wounds (often those left by the other species), but *C. hominivorax* is a true parasite. It only rarely lays its eggs in dead meat, although in the laboratory it will do so if the meat is at body temperature. As in other maggots that feed on living tissue, the floor of the pharynx is smooth, whereas in all carrion-feeding larvae the pharynx has longitudinal ridges, though nobody knows why.

Much of the recorded biology of screwworms up to 1933 really applies to *C. macellaria*, for *hominivorax* is rarely caught in carcass traps

Myiasis of Wounds and Natural Cavities (Screwworms) 751

but *macellaria* commonly is. The parasitic species occurs from the Gulf Coast states to Argentina. In the United States it normally survives the winter south of 30 deg. N. lat., but in cold winters only in small areas in Arizona, southern Texas, and Florida. It does not survive when the mean daily temperature falls below 49°F. for 3 months or 53°F. for 5 months; adults are killed below 20°, and pupae at 15°F. It has no true hibernation. It survives in wounds or in soil in warm winter weather and spreads gradually during a summer; after a mild winter it may have a good start towards further expansion the next summer. It may also be shipped to distant northern states with infested cattle in the spring, and cause local disturbances until winter comes. Since its pupae are adversely affected by moisture in the soil, it rarely establishes itself where the rainfall exceeds 4 or 5 inches a month.

The adult screwworm flies (Fig. 248A) are large, greenish blue flies with orange-red faces and eyes (see key, p. 743). The eggs are laid in batches of 150 to over 300, sometimes in more than one wound, and 8 or 10 such batches may be laid at intervals of 4 days. The incubation period is longer than that of *C. macellaria* and is seldom less than 12 hours. The larvae (Fig. 248B), are whitish with bands of minute spines; they can be distinguished from the larvae of *C. macellaria* by the much larger spiracles and large, heavily chitinized main tracheal tubes (Fig. 248C). Eating away at flesh and even bone, they grow to a length of 12 to 15 mm. when mature; they then spontaneously leave the animals, bury themselves in loose earth, and pupate. When infested animals die, the larvae leave within 48 hours and pupate under or within a foot of the carcass in the upper half-inch of soil. In experimental guinea pigs the maggots regularly mature and leave a wound on the fifth or sixth day. The pupal period is 7 to 9 days in summer but may be prolonged to 10 or 12 weeks in winter. *C. macellaria* may complete its whole life cycle in 9 or 10 days, but *C. hominivorax* is slower, requiring 18 to 22 days in summer weather.

Screwworms affect cattle, sheep, goats, and hogs most frequently, and may wipe out entire herds, for wounds once infested may be repeatedly reinfested. Human cases are rarer, but in 1935 there were over 100 human cases in the southern United States. In man the commonest site of infestation is the nose, whence the sinuses and nasopharynx are invaded, but the mouth, eyes, ears, vagina, and wounds are also attacked. Halitosis seems to be an attraction to screwworm flies as well as a repellent to romance, though the magazine advertisements have neglected to mention it. Sometimes *Dermatobia* lesions, boils, etc., are invaded, though more frequently by saprophagous species.

The damage done may be very extensive and is not infrequently fatal. Reports of 179 cases compiled by Aubertin and Buxton show that 15, or 8 per cent, died. There is usually an abundant discharge of pus, blood, and scraps of tissue, accompanied by intense pain. Often nervous conditions develop, such as delirium, convulsions, visual disturbances, and loss of speech.

Small numbers of larvae are fatal to laboratory animals; guinea pigs usually succumb to more than 3 per 100 grams of body weight. Evidently they are highly toxic and their damage is not limited to the tissue destruction they cause, though sometimes, when the infestation is in the head, this is bad enough. According to experiments by Borgstrom (1938), the maggots are invariably accompanied by proteolytic bacteria which aid them in attacking the tissues; there seems to be a symbiotic relation between them, the larvae killing the tissues with their toxins and making them available for the proteolytic enzymes of the bacteria, and the bacteria then decomposing the tissues to make them available for the larvae. After a day or two the wounds usually have pure cultures of these proteolytic bacteria (*Proteus*). In Florida, however, Emmel (1945) found screwworm flies to be vectors of "joint ill," a streptococcus condition of calves; the germs invade the body from navels infested by the maggots.

Immunity to the toxic effects of the infestation is developed, but, since the larvae do not feed directly on living tissue as does *Cordylobia*, there is no interference with growth of the larvae.

The damage done by screwworms to domestic animals amounts to millions of dollars in the United States. Wounds made by shears, barbed wire, thorns, ticks, parturition, etc., are commonly invaded, and myiasis of the cloaca of chickens is not infrequent. In our southern coastal areas from August to October about 12 per cent of cattle have infestations; during this season 85 per cent of all screwworm infestations begin in the bites of the Gulf Coast ear tick, *Amblyomma maculatum* (see p. 561). Next in importance are wounds made in shearing. Wounds made by castration, ear-marking, and branding are also important. The flies frequently oviposit in the sores made by bots, especially *Dermatobia* in cattle and *Cuterebra* in rabbits (see pp. 760 and 763).

THE OLD WORLD SCREWORM, *CHRYSOMYIA BEZZIANA*. This fly is widely distributed in Asia and Africa and has habits similar to those of *Callitroga hominivorax*, whereas its close relative, *Chrysomya megacephala*, is the counterpart of our *Callitroga macellaria*. *C. bezziana* is a common cause of human myiasis in India, but in Africa and in the

Philippines it confines its attentions largely to animals. The maggots are very destructive and cause horrible, stinking sores.

WOHLFARTIA MAGNIFICA. This fly, a member of the family Sarcophagidae (fleshflies) (see key, p. 743), is found in southeastern Europe, Asiatic Russia, and Asia Minor and has habits similar to those of the screwworms. It is a great pest in war, breeding in the wounds of soldiers. The eggs of this fly, as of other sarcophagids, hatch before being deposited. The young larvae are placed directly in the wounds or cavities which the fly chooses for them. According to Portchinsky 150 or more larvae are deposited at a time; one instance is recorded of 70 maggots being extracted from a human eye after about this many had already escaped or been thrown away. The larvae of *Wohlfartia* are larger than those of the calliphorine flies and so are capable of even greater damage.

Treatment and Control of Screwworms. When discovered, the larvae should be removed as speedily as possible, especially if in the head. In animals the wounds should be treated with a smear developed by the U. S. Bureau of Entomology called EQ 335, containing 3 per cent Lindane and 35 per cent pine oil, made up with mineral oil, emulsifier, and thickener (see Bruce, 1952). This is worked into the wound with a brush, and repeated in 5 to 7 days until the wound is healed. Substances like creosote, coal tars, etc., aggravate the wounds and retard healing.

In man removal of the maggots as soon as possible is indicated. Application of 5 per cent chloroform in a light vegetable oil or in milk is helpful if applied by douching for 30 minutes, or application of saturated dressings to wounds from which the maggots are not easily removed. Even salt water is helpful if no better wash is available. Infestations of the nose, sinuses, ear, etc., if not attended to promptly, may require surgery.

Control consists in treating infested wounds promptly and in taking all precautions possible against wounds, especially in the fly season. Spread of the infestation would be greatly curtailed if there were enforced examination and treatment of all animals before shipment from an infested area to a distant part of the country.

A novel method proposed by Bushland and Hopkins (1951), and successfully used in Curaçao in 1954, is the mass liberation of laboratory-reared male flies after sterilization by irradiation. A female fly mates only once, and if with a sterilized male none of her eggs will hatch. A male, on the other hand, may mate as many as eleven times if virgin females are available, so he may have a considerable effect on the next

generation. Preliminary tests indicate that if there are five to ten times as many sterile as normal males, there is very little reproduction. Since the fly survives the winter in rather small numbers and in limited areas, extermination in our southeastern states might be possible by the mass liberation of treated males over two winters and a summer. In Texas it would be more difficult because of the vast areas involved, and because of re-introduction from Mexico.

3. Wool Maggots Causing "Strike"

Sheep suffer from attacks by maggots which develop from eggs laid by carrion-feeding flies in damp wool soiled by feces or urine. Bacterial action produces ammonia, causes dermatitis, and attracts the flies. Such an infestation is called a "strike." The maggots eat into the flesh and often cause the death of sheep. Wool maggots are said to cause as much loss of sheep in parts of Australia as all other factors combined. Breeding in wool is a recently developed habit on the part of the flies—a result of changing conditions making for more blowflies, more vulnerable types of sheep, and perhaps less natural food for the flies. *Phoenicia* (or *Lucilia*) *cuprina* causes 96 per cent of the wool maggot trouble in Australia and is important, along with certain species of *Chrysomya*, in South Africa. In Europe the very closely related *P. sericata* is the species concerned. In Texas and California, the American states where "strike" is most frequent, the blue-black *Phormia regina* is the most important fleece worm.

Good control is obtained by dipping, power-spraying, or preferably high-power "jetting" of the crotch region of ewes and heads of rams with chlorinated hydrocarbons. Lindane, Dieldrin, and Aldrin are superior to the others because they diffuse along the wool fibers as the latter grow, and give protection for 6 months; the DDT group do not do this, and Chlordane does to a less degree.

4. Muscoid Skin Maggots

Two genera of muscoid flies, *Cordylobia* and *Wohlfartia*, pierce the skin of animals and develop in boil-like lesions in the skin after the manner of certain bots (*Dermatobia*, *Cuterebra*, and *Hypoderma*) which are discussed on pp. 760 and 763.

African Skin Maggots (*Cordylobia anthropophaga*). This yellowish brown fly (Fig. 249), called the tumbu fly, is related to the floor maggot (see p. 747) and, like it, is found throughout tropical Africa. Although rodents are probably the primary hosts, a large number of tender-skinned wild and domesticated animals, especially dogs, are attacked, and man is a frequent victim.

According to Blacklock and Thompson (1923) the eggs are laid by preference in dry sand and occasionally in cloth if either has been contaminated by excreta or has body odors, so clothing left exposed to flies may become dangerous. The eggs hatch in about 4 days. Upon stimulation by heat or touch the young larva becomes alert and active, attaches itself to skin, crawls to the nearest wrinkle or crevice, tears a hole with its mouth hooks, and within a minute or two has buried itself under the surface if the skin is not too tough. First attacks are painless, but there are marked reactions to subsequent attacks. The three larval stages (Fig. 250) are passed through in 8 days or more; the mature larvae then leave the tumor and pupate in the ground, the adult flies emerging after 8 or 10 days under favorable conditions.

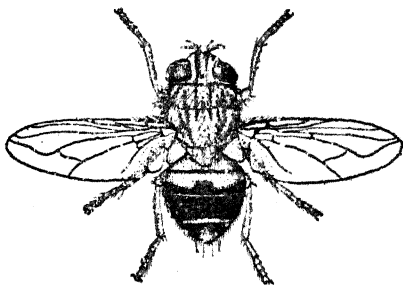


FIG. 249. Adult ♀ of African skin maggot, *Cordylobia anthropophaga*. $\times 3$. (After Castellani and Chalmers, *A Manual of Tropical Medicine*, 1920.)

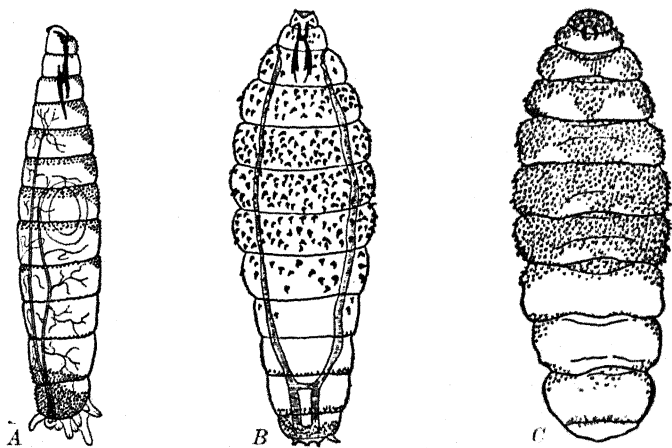


FIG. 250. A, B, and C, first-, second-, and third-stage larvae of *Cordylobia anthropophaga*; A, $\times 60$; B, $\times 15$; C, $\times 4$. (After Blacklock and Thompson, *Ann. Trop. Med. Parasitol.*, 17, 1923.)

Blacklock and Gordon (1927) made some interesting observations on immunity to this infestation, showing that larvae are unable to develop in previously infested skin. This the writer has interpreted as a specific

reaction of the skin tissue which makes it unavailable as food for the larvae. The immunity is local and temporary in nature, gradually spreading in the skin, and is retained even when immune skin is grafted into another animal.

The boil-like lesions are often considerably excavated, apparently by a histolytic action of the larvae, and heavy infestations in animals may even cause death.

Large maggots can be removed with forceps, but smaller ones are best removed by applications of liquid paraffin. The larvae back out into the paraffin searching for air and by addition of more drops can usually be induced to emerge far enough to be captured or squeezed out.

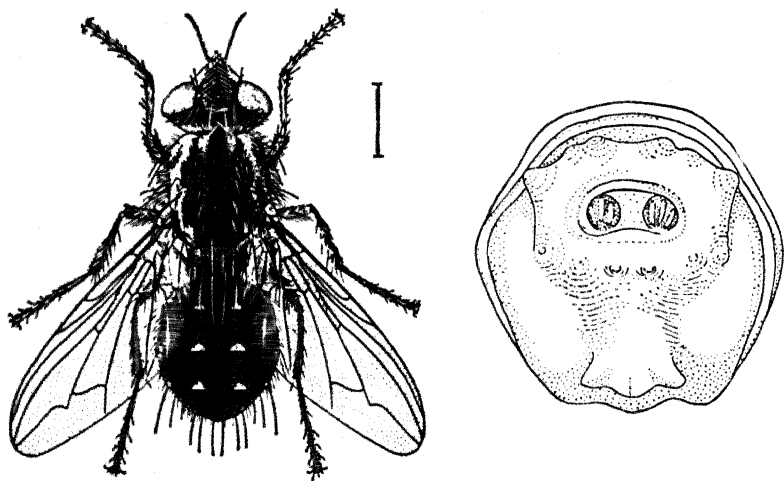


FIG. 251. Left, *Wohlfartia vigil*, adult ♀. (After James, U. S. Dept. Agric. Misc. Publ. 631, 1947.) Right, posterior end of third-stage larva of same. (Adapted from Walker, J. Parasitol., 7, 1920.)

***Wohlfartia vigil* and *W. opaca*.** Most of the species of *Wohlfartia*, like those of *Sarcophaga* (both members of the Sarcophagidae—see keys, pp. 743 and 745), are not primary myiasis producers, but, as we have already seen, *W. magnifica* is an Old World screwworm, and two American species, *W. vigil* and *W. opaca*, are invaders of healthy skin.

Walker in 1920 called attention to a number of cases of infestation of the otherwise healthy skin of young children by the maggots of *Wohlfartia vigil* (Fig. 251) in Toronto, Canada. Later, Ford (1936) reported additional human cases and many in small animals. In very small animals 5 to 20 larvae are said to cause death within 10 days. Young mink are frequently killed by them on farms in the upper

Mississippi valley. Ford observed that the female flies habitually deposit their larvae on the skin of animals, especially young and tender ones, when available; the larvae are unable to penetrate adult human skin.

Tender-skinned babies sleeping outdoors unscreened are liable to nasty infestations. Larval development is rapid, sometimes requiring only 5 days in hot weather but usually occupying 6 to 9 days. The majority of human cases have been reported from the Toronto region, but scattered cases have been noted in various localities in the west where *W. vigil* is replaced by *W. opaca*. This species, called the fox maggot, is a common and important parasite of foxes and mink in the west and causes losses running to thousands of dollars on farms where these animals are raised. Rarely, cases occur in dogs.

5. Myiasis of the Intestine and Urinary Tract

Intestinal Myiasis Many species of fly maggots may accidentally be taken into the intestine of man. To quote from Banks, "When we consider that these dipterous larvae occur in decaying fruits and vegetables and in fresh and cooked meats; that the blowfly, for example, will deposit on meats in a pantry; that other maggots occur in cheese, oleomargarine, etc., and that pies and puddings in restaurants are accessible and suitable to them, it can readily be seen that a great number of maggots must be swallowed by persons each year, and mostly without any serious consequences." The reason for the lack of serious consequences is the fact that most maggots are killed in the stomach and thus fail to establish themselves. This is rather surprising since the maggots are unusually resistant to many chemicals that would quickly destroy other animals. Causey in 1938 fed larvae of a number of species to dogs and cats and found the larvae to be killed or immobilized in the stomach within 3 hours; none of them passed through the alimentary canal alive. In another experiment fifty human volunteers were fed living maggots of *Musca domestica*, *Calliphora*, and *Sarcophaga* under conditions planned to avoid destruction in the stomach. Fifty per cent had gastro-intestinal disturbances—nausea, vomiting, cramps, and diarrhea—but the symptoms disappeared in 48 hours after elimination of the larvae, only a few of which were recovered alive after being vomited or passed in the feces.

Possibly intestinal myiasis is associated with low hydrochloric acid in the stomach or with particular conditions favoring rapid passage into the intestine. It is also possible that sometimes the flies get access to the intestine via the anus rather than the mouth, for some of the flies involved, particularly *Sarcophaga* and two species of *Fannia* (see

p. 743), normally deposit their eggs in feces and decaying organic matter, and their eggs or larvae would rarely be found in edible food.

Excluding the species of *Gastrophilus*, which are true parasites of the alimentary canal (see p. 766), all the fly larvae recorded as causing intestinal myiasis are accidental parasites and probably in most cases pseudoparasites, actually no more parasitic than a swallowed goldfish. Some workers doubt that any of the numerous species found in human feces stop to nourish themselves, much less multiply, en route, but the evidence is against this extreme view, for there are well-authenticated cases of digestive disturbances occasioned by them. Even if they do not attack the mucous membranes they may cause nausea and abdominal discomfort by their movements.

Occasional remarkable cases are recorded of long-standing infections, even when opportunities for reinfection do not appear to exist. There are reports of living larvae of fleshflies or their allies persisting and causing symptoms for periods of weeks or even months. Herms and Gilbert (1933) described a case in which the history suggested intestinal myiasis extending over many years. For 4 months larvae of *Calliphora*, *Phoenicia*, and *Sarcophaga* were found at intervals, accompanied by attacks of severe abdominal distress and intestinal hemorrhages. During this time the manner of life of the patient made the probability of repeated infection seem very remote. Lyon and Mizelle in 1945 reported a case in which *Phoenicia sericata* and an unidentified *Sarcophaga* were obtained from a woman who complained of having passed worms for a period of a month. Similar long-standing cases have been reported involving *Musca crassirostris* and the maggots of a small acalyptate fly of the genus *Aphiochaeta* (see p. 743).

Herms suggested the possibility of reproduction in the digestive tract by a process of pedogenesis, i.e., premature reproduction by larvae without transformation into adult flies. Such a method of reproduction is thought actually to have been observed by Parker in 1922 in a species of *Calliphora*. In some cases, however, it is a problem for a psychiatrist rather than an entomologist. The writer was once informed by a woman that she had been passing worms in her stool for over a year and suffering gastro-intestinal disturbances from them, and she brought a stool swarming with larvae of *Aphiochaeta* to prove it. She had been fascinated by seeing the larvae develop in stools saved in covered receptacles. When, however, a flytight jar was supplied for additional specimens, no more larvae were found.

The commonest fly maggots found in human feces are small species that breed in dead vegetable or animal matter, including *Piophilidae*, the cheese skipper (Fig. 252A and B); *Drosophila*, the fruit fly, famous

in genetics; *Aphiochaeta*; *Sepsis*; etc. The larvae of most of these have the posterior spiracles on tubercles but otherwise resemble miniature housefly larvae. Some, like the cheese skipper, can flick themselves about; the presence of this species is sometimes considered a mark of particularly good cheese.

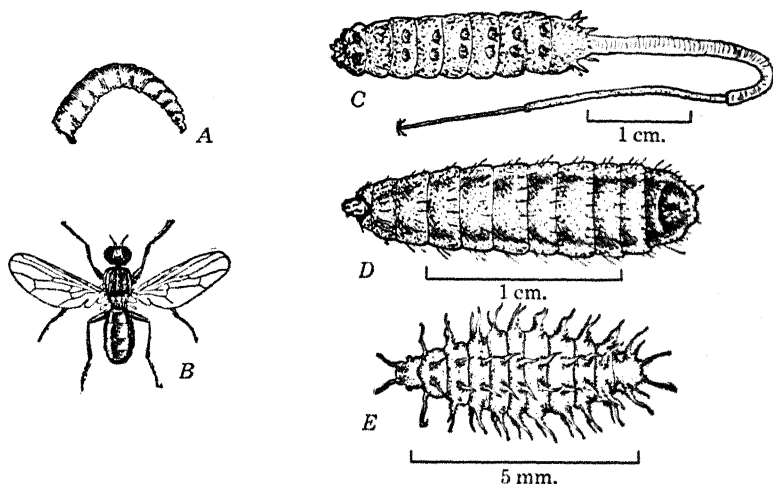


FIG. 252. Maggots occasionally found in human feces. A and B, cheese skipper and adult, *Piophilha casei*, $\times 3$. C, rat-tailed maggot, *Eristalis tenax*. D, *Hermetia illucens*. E, larva of lesser house fly, *Fannia canicularis*. (Adapted from various authors.)

Although undoubtedly harmless in most cases, these fly maggots sometimes damage the intestinal mucosa and cause loss of appetite, vomiting, colicky pains, headache, vertigo, etc. Other maggots occasionally found and connected with digestive disorder are two species of *Fannia* (Fig. 252E); *Musca domestica*; several species of fleshflies (*Sarcophaga*) (Fig. 253); rat-tailed maggots (*Eristalis*) (Fig. 252C); and a soldier fly, *Hermetia illucens* (Fig. 253D). The characteristics of these will be found on pp. 745 and 747.

Fly maggots can usually be expelled readily by means of the purges and various anthelmintics used for intestinal worms. Prevention, of course, consists principally in being careful of what is eaten, especially in regard to such foods as raw vegetables, cheese, and partly decayed fruits and meats.

Myiasis of Urinary Passages. Myiasis of the urinary passages, both urethra and bladder, is a rare but occasional occurrence. The flies implicated are usually the lesser housefly, *Fannia canicularis*, and

the closely allied latrine fly, *F. scalaris*. The writer in 1941 reported a case in which *Phoenicia* larvae were recovered. In most cases infection occurs from eggs laid near the external opening of the urethra, the larvae working their way up into this tube and even into the bladder; apparently they need very little oxygen. One case of infection of a boy's bladder by the larvae of a *Psychoda* was recorded by Patton; he

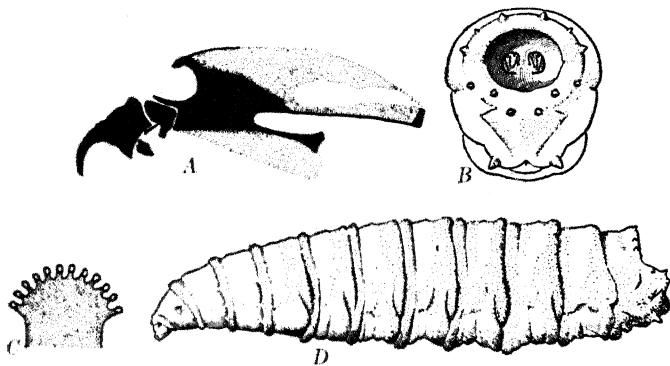


FIG. 253. Larva of *Sarcophaga crassipalpis*, a secondary wound invader. A, larva; B, posterior end of same showing stigmal plates in pit or recess; C, mouth hook and cephalo-pharyngeal skeleton characteristic of muscoid larvae; D, anterior spiracle. (A and B after James. C and D after C. N. Smith from James, U. S. Dept. Agric. Misc. Publ. 631, 1947.)

thinks that the larvae burrowed through from the rectum to the bladder. Hoeppli and Watt found that larvae of *Chrysomya megacephala* when placed in the urinary bladder taken from a freshly killed pig and filled with human urine, if fed daily, would live for 9 days, whereas *Phoenicia sericata* lived only 3 days. Contamination is favored by sleeping without covers in hot weather, giving flies free access to the anal and genital region.

BOTFLIES

I. Skin Bots (Cuterebridae)

The flies of this family are robust hairy flies distinguished from other bots (Oestridae and Hypodermatidae) by having a deep groove under the head containing a reduced proboscis.

***Dermatobia hominis*.** This big, blue, brown-winged fly (Fig. 254) is found from Mexico to northern Argentina. Its larvae develop in many animals, including cattle, dogs, hogs, goats, turkeys, and, more rarely, horses, mules, or man. The maggots of this fly, called "berne" in Brazil and "torsalo" in Central America, are undoubtedly the most

serious and damaging parasites of cattle in Central and South America. They retard growth, lower meat and milk production, cause anemia and digestive disturbances, and riddle hides until they become worthless. Human infestations are contracted chiefly in low forest regions and seldom in houses. Young children exposed outdoors may be severely affected, and occasionally are killed by them, as are cattle. Many calves are killed by secondary infestation by screwworms (see p. 749).

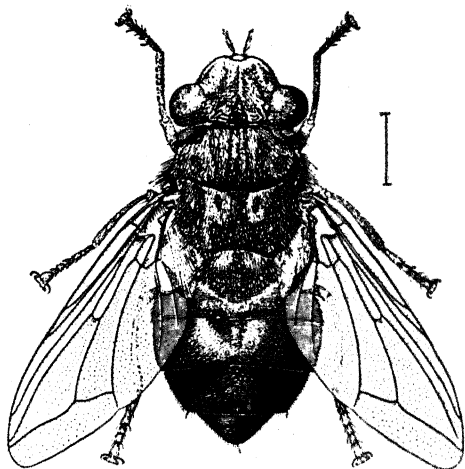


FIG. 254. *Dermatobia hominis* adult ♀. (After James, U. S. Dept. Agric. Misc. Publ. 631, 1947.)

The adult fly is about the size of a large blowfly, with the legs and face yellowish, the thorax bluish black with a grayish bloom, the abdomen a beautiful metallic violet blue, and the wings brown.

The method by which these flies give their offspring a start in life is unique. When ready to oviposit, the female captures an insect, usually a large mosquito of the genus *Psorophora* but occasionally various other Diptera or even ticks, and glues her eggs by means of an adhesive, quick-drying cement to the underside of the abdomen of her captive (see p. 734 and Fig. 243). A total of 200 eggs may be laid by one female fly, 8 or 10 to several dozen on individual mosquitoes. The eggs require several days' incubation before they are ready to hatch.

When mosquitoes burdened with ripe eggs alight upon the skin of warm-blooded animals the maggots emerge, penetrate the skin of the host, and begin their development. If the young larva does not have

time to emerge while its mosquito transporter is biting it is said to draw back into the egg shell and await another opportunity.

The larvae mature in the host's skin in 5 to 10 weeks. They ultimately reach a length of 18 to 24 mm. (Fig. 255). The anterior end of the larva is broad and is provided with double rows of thorn-shaped spines; the posterior portion is slender, smooth, and retractile. As the larva develops, a boil-like cyst forms about it, opening to the surface of the skin by a little pore which is plugged by the posterior end of the maggot and is used for obtaining air. At intervals these

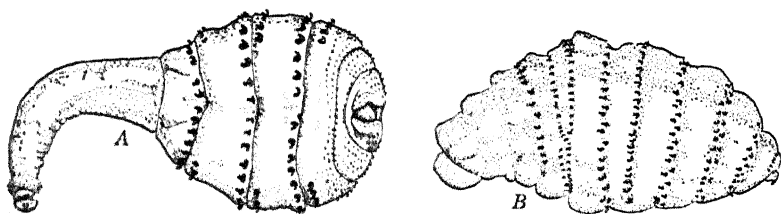


FIG. 255. *Dermatobia hominis*: A, first-stage larva; B, third-stage larva. (A adapted from Blanchard, from Neveu-Lemaire, *Traité de zoologie médicale et vétérinaire*. II. Entomologie, Vigot Frères. B, original.)

warble-like boils cause excruciating pain. When mature, the larvae voluntarily leave their host and fall to the ground to pupate. They transform into the adult form in the course of several weeks; the entire life cycle requires 3 to 4 months.

After the worms have evacuated their cysts or have been removed, the wounds sometimes develop serious or even fatal infections, or are invaded by screwworms. To remove the maggots, frequently tobacco juice or tobacco ashes are applied to the infested spots, thus killing the worms and making their extraction easy. Another method used by natives in some parts of South America is to tie a piece of fat tightly over the entrance to the boil. The larva, deprived of air, works its way out into the fat, being thus induced to extract itself. A much more satisfactory method is to enlarge the entrance to the cyst with a sharp clean knife and remove the worm with a forceps. Antiseptic treatment of the wound obviates danger of subsequent infection. The wound heals quickly but leaves a scar. Treatment of *Dermatobia* lesions in animals with smear EQ 335 (see p. 753) or 4 per cent Lindane in lubricating grease and used engine oil is very effective.

Good control is obtained by spraying animals with Toxaphene or Lindane, using 1 qt. of 0.5 per cent emulsion or suspension twice monthly. On one farm in Nicaragua about 850 *Dermatobia* larvae

were extracted per animal during 9 months preceding treatment; 9 months *after* treatment there was less than 1 per animal and no *Boöphilus* ticks (Laake, 1953). Hypodermic injection of 10 mg. per kg. of Lindane at intervals of 20 days, or addition of that amount to food at those intervals, reduced the infestation per animal very markedly (de Toledo and Bauer, 1950).

***Cuterebra* spp.** This genus contains a number of species of large bee-like flies the larvae of which develop individually in the skin of rodents and rabbits, fairly frequently in cats, and rarely in dogs. The full-grown larvae are large robust maggots, sometimes over an inch long; they are easily recognized by their complete covering of black spines which gives them a jet-black color. The younger instars have only rings of spines. Usually an animal harbors only one or a few maggots, but occasionally there are more.

According to Dalmat (1942) the flies lay very large numbers of eggs, depositing them in the burrows or habitats of the host, where they hatch intermittently. The larvae attach themselves to a host when the opportunity comes. They live in the host about a month and have a long pupal period in the soil; probably there is usually only one brood a year.

The maggots seem to be definitely injurious to their hosts, sometimes causing parasitic castration. *Cuterebra* lesions in cats and dogs are remarkably dirty and persistent. Most screwworm infections in rabbits develop in *Cuterebra* sores. Infested squirrels are considered inedible by hunters and are thrown away.

2. Bots Causing Warbles in Cattle (*Hypoderma* spp.)

***Hypoderma*.** The warble or heel flies, *H. bovis* and *H. lineata* (see key, p. 744, and Fig. 256), are hairy, black and yellow flies which lay their eggs on the hairs of the lower part of the legs or flanks of cattle, causing them great annoyance. The annoyance is purely instinctive, for the flies do not bite or sting, yet the animals act terror-stricken. One fly may deposit 100 or more eggs on one animal. The eggs hatch in a few days; the spiny larvae, 1 mm. long, burrow into the skin, and then for several months they ramble about among the viscera in the abdomen and thorax. Those of *H. lineata* commonly invade the walls of the esophagus and only occasionally enter the spinal canal, whereas for *H. bovis* the reverse is true. During this migratory phase the larvae are glassy smooth and grow to a length of 12 mm.

Toward the end of the winter they begin to appear in the skin of the back, where they form little cyst-like lumps or warbles. The larvae

(Fig. 256, right) develop in the warbles for about 1 to 3 months, molt twice, and become opaque, warty maggots which make a little breathing hole in the skin, into which they thrust the posterior end with its spiracles. The warbles usually appear in early December in the South, in mid-February in the north. The grubs usually emerge in spring or early summer, fall to the ground, and pupate. The pupae are very resistant to cold but are killed by excessive moisture. The adults emerge in 2 to 7 weeks. They have a flight range of about 3 miles.

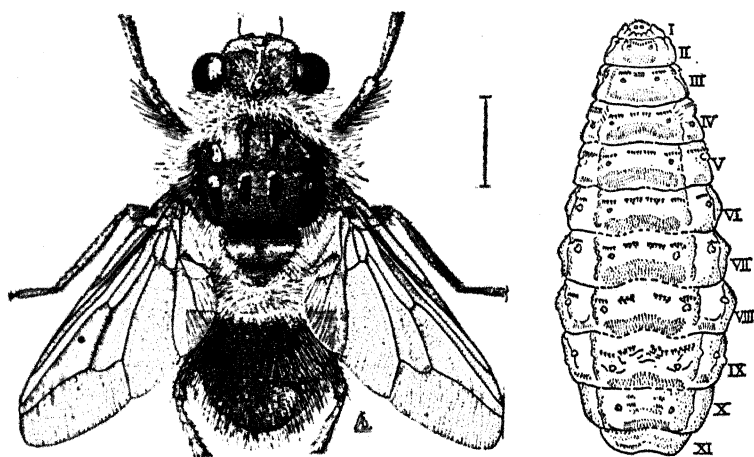


FIG. 256. Left, common cattle grub or warble fly, *Hypoderma lineata*, adult ♀ (after James, U. S. Dept. Agric. Misc. Publ. 631, 1947). Right, third-stage larva of same (after Cameron, *Trans. Highland and Agric. Soc. Scotland*, Ser. 5, 49, 1937, from James).

The two species in cattle, *H. bovis* and *H. lineata* (see keys and Fig. 246), are much alike in their biology, but *H. bovis* appears about a month later than *H. lineata* in all its stages. In the United States this species is limited to the northern and central states. *H. crossii* of Indian goats is said to undergo its entire development in the subcutaneous skin of the back.

Hypoderma larvae are occasional accidental parasites of man, but being in an abnormal host they do not behave in a normal manner but wander aimlessly in the skin, causing "migrating lumps." *H. diana* of deer in Europe is a more frequent accidental parasite of man than are the cattle species. *Hypoderma* has been reported to cause myiasis of the human eye in Norway and Russia.

Warbles cause losses amounting to millions of dollars by irritation to cattle caused by the larvae, annoyance caused by the flies, and damage to hides.

Since there is no wild-animal reservoir for the cattle grubs, community effort has brought about great reduction of it in many places, even before the advent of modern insecticides, when hand removal of the grubs or individual treatment of the warbles was necessary. By continued effort and broadening of control areas, extermination would be possible, and then *Hypoderma*, like *Boöphilus*, would be only a memory in this country. The most effective insecticide is rotenone (see p. 515), applied to the backs of cattle when the warbles are present, either by power spraying, dusting, hand-applied washes, or ointments. Using derris or cubé powder containing 5 per cent rotenone, good washes contain 1 lb. per gallon, sprays 1 lb. per 10 gallons, dusts or ointments about 1.5 per cent rotenone. Since only the backs are infested, dips are less economical. The rotenone should first be applied 30 to 40 days after the first appearance of the warbles, and then every 30 to 40 days during the season. Ingestion of phenothiazine in salt mixtures reduces the number of grubs by about 85 per cent.

3. Head Bots (Oestridae)

The family Oestridae contains robust flies with a hairy "pile" of black, yellow, or gray. These, while on the wing, deposit their newly hatched larvae (or eggs in some species) in or on the nostrils of sheep, goats, deer, and camels, or, rarely, in man. The larvae are large grubs an inch or more in length. The important species are *Oestrus ovis*, a world-wide parasite of sheep and goats, *Rhinoestrus purpureus* of horses in the Old World, *Cephalopina tiillator* of camels in North Africa and Asia, and *Cephenemyia* spp. of members of the deer family in North America and Europe.

***Oestrus ovis*.** The larvae of this grayish brown fly, imported from Europe, are a pest in southwestern United States, where over 95 per cent of sheep and goats are infested. The flies deposit their larvae in the nostrils. The young larvae live in the nares, but later invade the frontal sinuses and sometimes other parts of the head. Occasionally they find their way into the tear duct and reach the eye, sometimes destroying it. They develop slowly through the winter and mature and drop out in the following spring or summer. In Canada the average pupal period is about one month. In warm countries there may be two broods, adults appearing in May and June and again in October and November. The full-grown larvae are over an inch long with characteristic spiracles (see Fig. 246).

The irritation caused by the grubs makes the animals restless and they stop feeding. They develop a nasal discharge and sneeze frequently. The parasites can be reached most easily while in the nares

during the winter. Treatment by intranasal injections of 3 per cent saponified cresol or 25 per cent tetrachlorethylene emulsion has been recommended. Sometimes a violent sneeze brought on by the use of pepper will expel them. Smearing the noses with pine tar or getting sheep to smear their own noses by placing salt in 2 to 3 in. holes in a smeared log provides some prevention.

This fly sometimes deposits its eggs on the eyes, nostrils, and lips of shepherds whose breath smells of fresh sheep or goat cheese or curds. The grubs may cause serious damage to the eyes.

Other Oestridae. The larvae of the purplish-hued *Rhinoestrus purpureus* are frequent parasites of the head of horses in Europe, Siberia, and north Africa. Like the sheep bot, this fly sometimes darts at human beings and deposits its larvae in the eyes, where they may cause serious damage if not promptly removed. One oestrid, *Booponus intonosus*, the hoof maggot of Celebes and the Philippines, lays its eggs on the feet of cattle and the larvae develop there.

Cephalopina titillator causes great discomfort to camels; it lives in the nostrils and nasopharynx for 10 or 11 months. The deer head-bots, *Cephenemyia* spp. (sometimes placed in the family Cuterebridae), are well known to hunters. Nearly all deer are infested by them, but they seem usually to do little damage, though sneezing fits are sometimes observed as are occasional cases of "eraziness," possibly due to rare penetration of the parasites into the brain. The adults of *Cephenemyia* are among the swiftest flying insects known; they are said to get up a speed of 800 miles an hour. Females are rarely seen. The males of our western *C. jellisoni* rest on sun-warmed rocks on inaccessible mountaintops. Bagging one is more of a feat for a hunter than getting a mountain goat or a condor; when found in their remote retreats they have to be shot with .22-caliber dust shells!

4. Horse Bots (*Gastrophilus* spp.)

The genus *Gastrophilus*, constituting a separate family Gastrophilidae (see key, p. 744), contains flies the larvae of which develop in the stomach or rectum of horses. The adults are hairy bee-like flies, clothed in dark brown or black with yellow markings, and one species has an orange-red tip to the abdomen (Fig. 257, 4). The wings of the commonest species, *G. intestinalis*, have smoky markings (Fig. 245, 6). The abdomen in the females is elongated.

Each of the species has somewhat different habits, but all cause an amazing amount of annoyance while laying eggs, the horses becoming excited and often frantic; on warm days a horse may be so worried fighting botflies (gadflies) that he cannot graze at all. The adults

usually live for only about 3 to 10 days, but during that time a female lays several hundred eggs which she attaches to hairs on parts of the horse which vary with the insect species. *G. percorum* is an exception (see below). The first-stage larvae (Fig. 257, 2) have rings of black spines; third-stage larvae (Fig. 257, 5) are heavy-bodied and rather

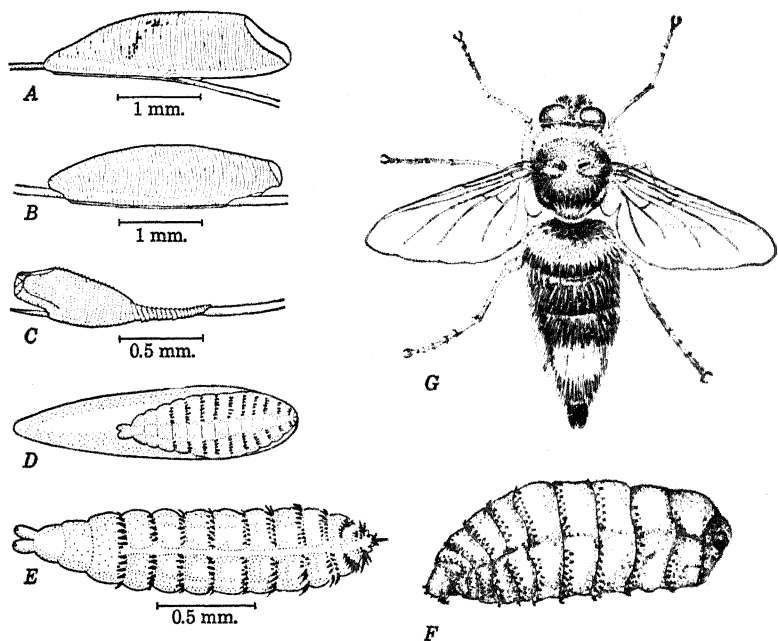


FIG. 257. *Gastrophilus*. A, egg of *G. intestinalis*; B, egg of *G. nasalis*; C, egg of *G. haemorrhoidalis*; D, egg membrane enclosing unhatched larva of *G. intestinalis*; E, first-stage larva of same; F, third-stage larva of same; G, *G. haemorrhoidalis*. (A-E and G adapted from Hadwen and Cameron, *Bull. Ent. Research*, 9, 1918.)

squarish posteriorly; all but *inermis* have heavy spines on some of the segments—one row in *nasalis*, two in the others. In *G. intestinalis* the spines of the first row are larger than those of the second (Fig. 257, 5), and vice versa in *haemorrhoidalis*.

The common horse bot, *G. intestinalis* (*equi*), lays its eggs on the hairs of the fore legs of the horse, where they incubate for 1 to 2 weeks. When ripe, the warmth and moisture of the animal's tongue when licking cause them to hatch and adhere to the tongue. In the mouth they excavate tunnels under the mucous membranes, principally of the tongue, and after 3 or 4 weeks migrate to the stomach, where they

live, often in large colonies, until mature and ready to pupate. They then release their hold and are passed in the droppings.

G. haemorrhoidalis (nose fly) (Fig. 257, 4) strikes at the lips to lay its eggs. The young larvae burrow about in the lips and tongue, later developing in the stomach and duodenum. This species leaves these parts in early spring and finishes its development in the rectum. *G. nasalis* (chin fly) lays its eggs on the chin and throat, where they hatch unaided. The larvae crawl to the lips to enter the mouth, and invade spaces around and between the teeth, below the gums, causing pus pockets. They may live in this locality for a month and undergo their first molt before they continue on their way to their final site of development in the lower stomach and duodenum. *G. inermis* lays its eggs on the cheeks, where it causes a dermatitis; the larvae burrow through the tissues to the mouth and then go to the rectum. *G. pecorum* lays its eggs on the hoofs sometimes, but usually on food or in pastures. When the eggs are ingested they hatch in the mouth, burrow into the mucosa, make their way to the esophagus and stomach, and eventually go to the rectum and re-attach before finally leaving the body.

A few horse bots do very little damage, and some farmers think that a horse just naturally ought to have a few, but when numerous the bots cause gastro-intestinal disturbances. The worms in the stomach are persuaded to let go by giving carbon bisulfide in gelatin capsules at the rate of 1.5 drams per 250 lb. of horse. Toluene given by stomach tube (10 ml. per 100 lb.), being tested against *Ascaris* in horses, was found by Todd et al. to be very effective against *G. intestinalis* but less so against *G. nasalis*.

Gastrophilus occasionally penetrates into man, but instead of behaving in an orthodox manner, the larva wanders about under the skin and is called a "larva migrans." *G. intestinalis* is the most common species concerned in this.

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